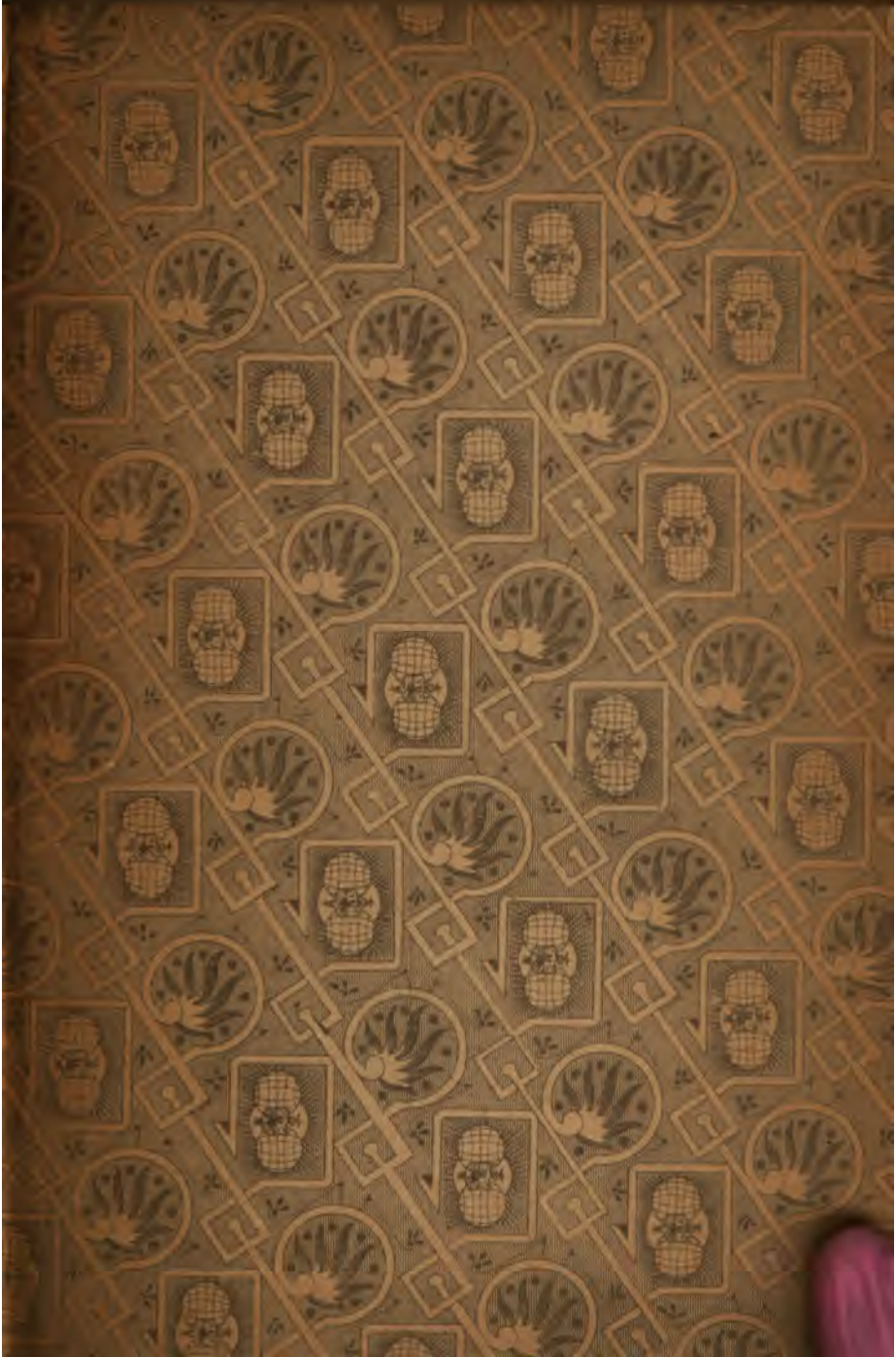

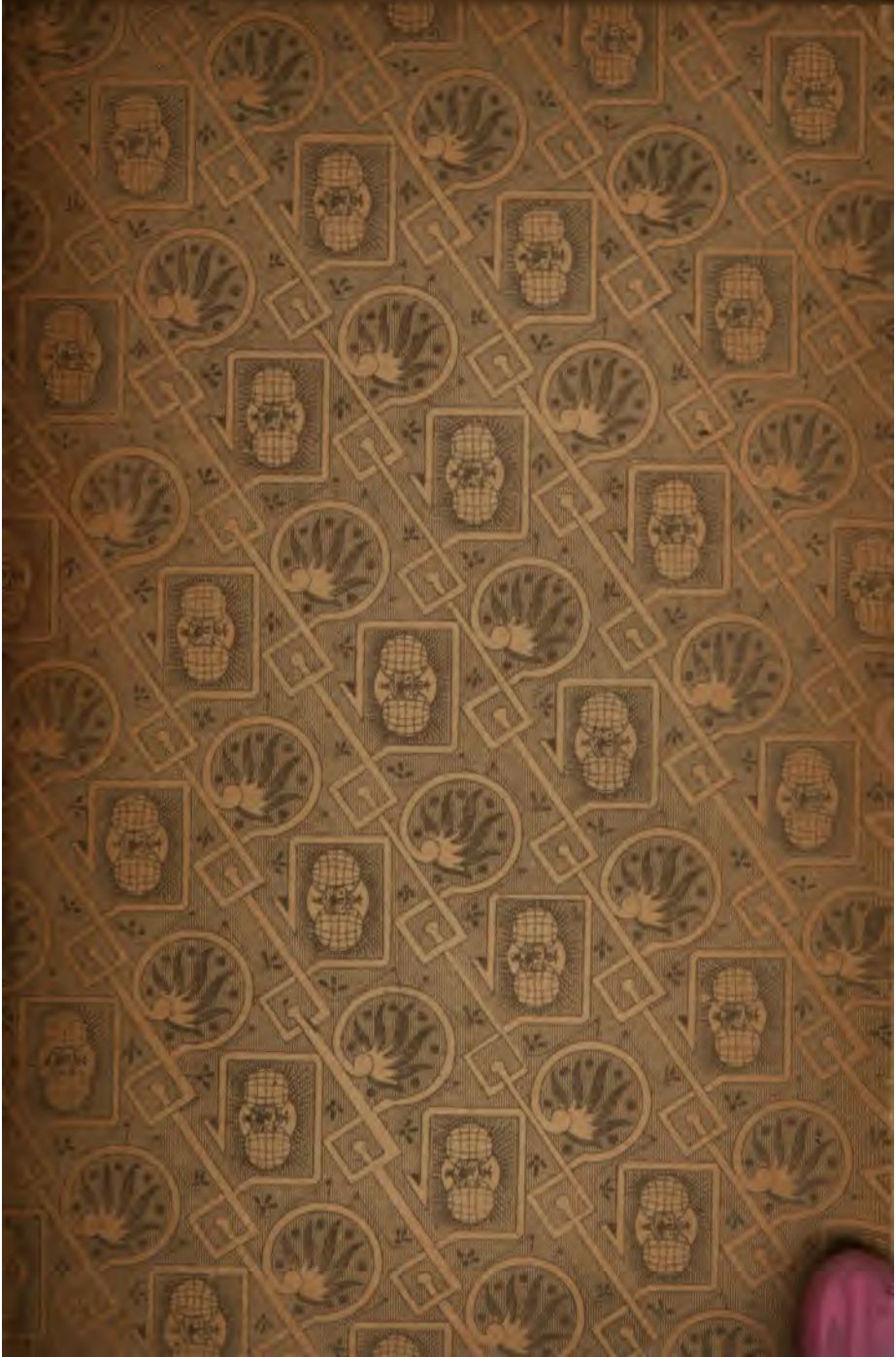

No. 8 IN THE PHYSICIANS' AND STUDENTS' READY REFERENCE SERIES.

DIABETES:

ITS CAUSES, SYMPTOMS, AND TREATMENT.

BY

CHARLES W. PURDY, M.D.,

QUEEN'S UNIVERSITY,

Honorary Fellow of the Royal College of Physicians and Surgeons, Kingston; Member of the College of Physicians and Surgeons of Ontario; Author of "Bright's Disease and Allied Affections of the Kidneys;" Member of the Association of American Physicians, of the American Medical Association, of the Chicago Academy of Sciences, of the Illinois State Microscopical Society, etc., etc.

WITH CLINICAL ILLUSTRATIONS.

PHILADELPHIA AND LONDON:

F. A. DAVIS, PUBLISHER,

1890.

Philadelphia:
The Medical Bulletin Printing House,
1231 Filbert Street.

TO

Thomas Grainger Stewart, M.D., F.R.S.E.,

PHYSICIAN IN ORDINARY TO HER MAJESTY THE QUEEN FOR SCOTLAND, PRESIDENT OF THE ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH, PROFESSOR OF PRACTICE OF PHYSIC AND OF CLINICAL MEDICINE, UNIVERSITY OF EDINBURGH,

AS A TOKEN OF

HIGH PERSONAL ESTEEM

AND IN

REMEMBRANCE OF NUMEROUS PROFESSIONAL FAVORS AND PERSONAL KINDNESSES,

THE FOLLOWING PAGES ARE INSCRIBED BY

THE AUTHOR.

PREFACE.

THE object of this volume is to furnish the physician and student with the present status of our knowledge on the subject of diabetes in such practical and concise form as shall best meet the daily requirements of practice, as they seem to me from a careful study and recorded observation of the disease extending over a period of twenty-one years.

I have dwelt with some minuteness upon the treatment, more especially in matters of diet, well knowing that a disregard of these details constitutes the most frequent cause of failure in controlling the disease. In order to further elucidate this part of the subject, I have illustrated the various forms of the disease with their appropriate treatment from cases in actual practice, selected from my clinical records.

Finally, I have endeavored to bring out prominently the leading features of diabetes as it occurs in the United States, together with the natural resources of the country best suited to the disease, as the waters, foods, and climate, since the very extensive range of these entitles them to rank in point of efficiency for the relief of the diabetic patient as at least equal to those in any other land or clime.

THE AUTHOR.

163 STATE STREET,
September, 1890.

CONTENTS.

SECTION V.

SECTION VI.

SECTION VII.

SECTION VIII.

DIABETES.

SECTION I.

DIABETES MELLITUS.

HISTORICAL, GEOGRAPHICAL, AND CLIMATOLOGICAL CONSIDERATIONS.

WE have reasons to believe that diabetes was known in periods of remote antiquity. The earliest records of the disease come from India. In the Ayur Veda of Susruta is to be found the following passage*: "Mellita urina laborantem quem medicus indicat, ille etiam incurabilis dictus est." The presence of the disease in various parts of Europe and Asia during very remote periods is referred to by numerous writers, although nothing definite upon the subject is to be found in the extensive writings of Hippocrates. Celsus, who lived nineteen hundred years ago, wrote: "If the quantity of urine which is passed is larger than the quantity of liquids imbibed . . . . emaciation is caused, and life is endangered."

Both Galen and Aretæus speak of the disease in several passages, but the latter especially has described it minutely, and was one of the first to use the name "diabetes." He wrote: "The patients urinate unceasingly . . . . they are tortured by an unquenchable thirst; they never cease drinking and urinating . . . . the integuments of the abdomen become wrinkled, and the whole body wastes away."

*Hirsch's Hand-book of Historical Pathology, vol. ii, p. 643.

During the middle ages writers have made repeated mention of a disease characterized by excessive flow of urine, thirst, and wasting, which must have referred to diabetes; but none of them speak of the sweet properties of the urine. This peculiarity of the urine, if known, seems to have escaped notice until about two hundred years ago, when Thomas Willis first called attention to it.* It was not, however, until one hundred years later (1775) that Dobson† first showed that the peculiar taste of diabetic urine depended upon sugar, which he demonstrated by evaporating the urine and producing the sugar in crystals. About twenty years later John Rollo published a systematic essay on diabetes, minutely describing a number of cases, and his thorough discussion of the subject laid the foundation of its subsequent literature.

The geographical distribution of diabetes embraces the widest possible range, with few exceptions, including every land and clime. The records show a greater frequency of the disease in certain locations than in others, but precisely how much this depends upon climatic conditions has, up to the present time, been undetermined by systematic observation.

The disease appears to be rare in St. Petersburg, as attested by Attenhofer and Lefévre, the former not having seen a case in his practice, or heard of one in that of his colleagues, for six years. Similar accounts come from Copenhagen, where no records of death from diabetes occur in the mortality tables from 1835 to 1838. We have records of cases from Turkey and Egypt, and in Morocco the disease is not uncommon. No mention of the disease is made by the English or French phy-

* Pharmaceutice Rationalis, sec. iv, chap. iii, p. 64.
† Med. Observer and Inquirer, London, 1776, v, 296.

sicians in their practice on the Coast of Guinea. On the other hand, the disease is remarkably common in Ceylon and in some parts of India, notably in Bengal. From China, Japan, Australia, and the islands of the Pacific we have no authoritative records of the disease; and the same may be said of Central America and the West Indies. Blair declares that in Guiana it is absolutely unknown. In Mexico it is met with quite often, but in Brazil it seems to be little known.

The following table, the data of which is taken from "Hirsch's Hand-book," gives in an incomplete way the distribution of diabetes throughout Europe:—

TABLE I.

LOCATION.	Period.	Deaths from Diabetes per 1000 Deaths.
England	1852 to 1869	1.25
Ireland	1841	.74
Schleswig Holstein	1871 to 1879	.65
Berlin	1877 to 1879	.94
Chemnitz	1871 to 1874	1.00
Frankfort-on-the-Main	1865 to 1880	1.60
Wurzburg	1852 to 1855	1.20
Brussels	1864 to 1880	.60

With regard to the climatology of diabetes, Dr. Dickinson, who has studied the subject closely in Great Britain, concludes that the disease is more common in the colder counties of the kingdom than in the warmer ones.

It has seemed to me that our own country offers exceptional advantages for climatic study of diabetes. The United States comprises a territory of about 3000 miles in length by about 2000 miles in width. Its area is over three and a half millions of square miles—nearly equal to the whole continent of Europe—or

twenty-nine times larger than Great Britain and Ireland. It possesses all ranges of mean temperatures for the year, from 35° F. in Vermont, to 75° F. on the Gulf coast; all elevations from the sea-level to an altitude of 10,000 feet and over; all ranges of rain-fall for the year from 10 to 60 inches. It will be readily perceived, therefore, that such a wide range of geographical and climatic features enable us to give an emphatic answer to many questions relating to the influence of climate over disease, which has proved to be exceedingly baffling in those countries possessing a more limited area and range of climate.

In attempting a systematic study of the climatology of diabetes in our own country, I was first met by the unfortunate fact, that the United States, unlike all other civilized nations, has no system of registration of vital statistics. The data afforded by the census is, therefore, the chief source from which even an approximate estimate can be made of liability to particular forms of disease in different parts of the country. Fortunately, an effort has been made in the last census (1880) to obtain more complete and accurate returns of deaths than have before been furnished, and likewise to make the returns more accurate as regards the causes of death. With regard to diabetes, the deaths have been reported under the head of "glycosuria," and, therefore, cases of non-saccharine urine—diabetes insipidus—do not vitiate the records.

In order to insure greater accuracy in calculations, I have excluded from my records and tables all States and Territories furnishing a total death-list of less than 5000; because the comparatively low mortality from diabetes—.5 to 6. per 1000 deaths—renders estimates on a lower basis necessarily very faulty. I have compiled the fol-

lowing table (No. II) chiefly from the mortality reports of the tenth census of the United States, ending with the month of May, 1880 :—

TABLE II.—*Deaths from Diabetes per 1000 Deaths in each State in the United States in 1880.*

STATE.	Total Deaths.	Deaths from Diabetes.	Rate per 1000.
Alabama	17,929	10.	.55
Arkansas	14,812	11.	.70
California	11,530	23.	1.99
Connecticut	9,179	31.	3.37
Georgia	21,549	24.	1.11
Illinois	45,017	98.	2.11
Indiana	31,213	85.	2.72
Iowa	19,377	47.	2.42
Kansas	15,160	24.	1.58
Kentucky	23,718	41.	1.31
Louisiana	14,514	15.	1.03
Maine	9,523	42.	4.41
Maryland	16,919	19.	1.12
Massachusetts	31,149	65.	1.96
Michigan	19,743	53.	2.68
Minnesota	9,037	16.	1.99
Mississippi	14,583	13.	.88
Missouri	36,615	52.	1.42
Nebraska	5,930	10.	1.68
New Jersey	8,474	10.	1.18
New York	88,332	195.	2.20
North Carolina	21,547	25.	1.11
Ohio	42,610	139.	3.23
Pennsylvania	63,881	116.	1.81
South Carolina	15,728	10.	.63
Tennessee	25,919	44.	1.69
Texas	24,735	19.	.76
Vermont	5,024	32.	6.36
Virginia	24,681	29.	1.13
Wisconsin	16,011	45.	2.81

It may first be noted that the mortality reports of the United States census for 1880 give a total mortality for the country from all causes of 756,893. Of these, 1443 were returned under the head of glycosuria. This gives an average ratio of deaths from diabetes for the whole country of 1.90 per 1000 deaths.

The most notable feature brought out by Table II is the comparatively enormous mortality from diabetes in the State of Vermont—6.36 per 1000 deaths,—so far as I am aware, the highest ratio of any place in the world. Now, the chief features of the climate of Vermont are the long-continued and severe winters. The snow remains on the ground from five to six months of the year, and the mean range of temperature is only about 35° F. The State of Maine, which adjoins Vermont on the north and east, and the climate of which is little, if any, less severe than that of the latter, furnishes the next highest mortality from diabetes in the United States—4.41 per 1000. While there can be little doubt that the severity of the climate in these two northeastern States is chiefly responsible for the high mortality from diabetes, it yet remains to account for the difference in the mortality between these two States lying side by side. It is true that Maine borders on the sea, but three-fourths of the State is as far removed from the sea as Vermont. What, then, determines the difference in the mortality from diabetes between these two States? I have no doubt, as I shall hereafter endeavor to show by numerous illustrations, that it is largely, if not solely, determined by altitude. It is perfectly clear to me that diabetes is a more fatal disease in higher altitudes, and this holds true in any latitude. Under diminished atmospheric pressure oxidation is greatly impeded, and under such circumstances the disease will prove more fatal. It must not be forgotten that the amount of oxygen in the system, and consequently the activity of oxidation in the economy, depends not upon the quantity of oxygen in the atmosphere, but directly upon the degree of atmospheric pressure. Thus, Demarquay has shown that the blood of people who dwell

in a locality where the atmospheric pressure is only 380 millimetres contains but one-half as much oxygen as the blood of those who live at the sea-board, where the atmospheric pressure is 760 millimetres. Now, the effect of increased oxidation in the system is undoubtedly a favorable one in diabetic conditions, whether it be brought about by increased atmospheric pressure through residence near the sea-level, or by the more direct way of inhalations of oxygen gas; indeed, the latter has reduced remarkably—one-half—the quantity of sugar in the urine of diabetics without any associated change of diet.

The State of Vermont, in addition to being one of the coldest States in the Union, has for the most part an elevation above the sea of from 3000 to 5000 feet, while its neighbor, Maine, lies comparatively low. It is true that Maine is largely hilly and broken country, but only a comparatively small part of the State in the west and north rises into mountains.

It may then be safely assumed that cold and altitude are the chief climatic features that determine high mortality from diabetes. If we pass to the south sufficiently far to reach the highest mean annual temperature of the country,—say 75° F.,—and select a State at or near the sea-level, such as Alabama, we find that the mortality from diabetes sinks to the lowest ratio in the country—.55 per 1000 deaths.

In order, however, to reach more accurate conclusions as to climatic influences over diabetes, it is better to group together certain tracts of country whose climatic features in each group are as nearly alike as possible. With this end in view I have adopted the grouping of Mr. Gannott, the geographer of the Census Office, since it seems to me altogether the best that has

TABLE III.—*Deaths from Diabetes per 1000 Deaths in United States in 1880, in Grand Groups, showing Mean Annual Temperature, Rain-fall, Elevation, and Population of each Grand Group.*

REGION.	Deaths per 1000 Deaths.	Mean Temperature.	Mean Rain-fall.	Elevation.	Population.
1. North Atlantic Coast Region	2.91	40°–50° F.	40–50 inches.	100– 500 feet.	2,616,870
2. Middle Atlantic Coast Region	.98	45°–60° F.	45–55 "	Below 100 "	4,376,135
3. South Atlantic Coast Region	.76	60°–65° F.	50–60 "	" 100 "	876,086
4. Gulf Coast Region	.88	70°–75° F.	55 "	" 100 "	1,056,034
5. Northeastern Hills and Plateaus	3.98	35°–45° F.	35–45 "	500–6000 "	1,669,229
6. Central Appalachian Region	2.47	40°–45° F.	35–40 "	Above 500 "	2,344,089
7. Northern Lake Region	2.31	45°–50° F.	30–40 "	" 800 "	3,049,402
8. The Interior Plateau Region	2.17	45°–50° F.	40–45 "	100– 200 "	5,714,683
9. Southern Central Appalachian Region	1.88	45°–55° F.	45–50 "	500–2000 "	2,698,958
10. Ohio River Belt Region	2.40	45°–50° F.	45–50 "	500–1000 "	2,440,339
11. Southern Interior Plateau Region	.87	65°–70° F.	50–60 "	Below 1000 "	3,625,545
12. Northern Mississippi River Region	2.50	40°–50° F.	30–50 "	Above 500 "	1,990,917
13. Southwest Central Region	.94	60°–70° F.	35–50 "	100– 500 "	2,932,676
14. Prairie Region	2.42	50°–55° F.	25–40 "	1000–2500 "	5,721,836
15. Northwestern Region	2.74	40°–50° F.	30–40 "	1000–1500 "	1,123,419
16. Pacific Coast Region	2.98	45°–65° F.	20–60 "	100–3000 "	715,781

been attempted. With this as the basis I have, from various sources, worked out Table III, which gives the death-rate from diabetes per 1000 deaths, the mean annual temperature, the mean elevation, and the population of each group. The topography of these groups is given below:—

"NORTH ATLANTIC COAST REGION comprises a strip of land from 50 to 75 miles wide, along the coast of Maine, New Hampshire, Massachusetts, Rhode Island, and Connecticut. The surface is mainly undulating and hilly, becoming less varied toward the south. The coast is bold and rocky in Maine, but mostly sandy and low in Massachusetts, Rhode Island, and Connecticut. There is little swamp or undrained land. The elevation is from 100 to 500 feet.

"THE MIDDLE ATLANTIC COAST REGION includes a strip of land comprising the coast counties of New York, New Jersey, Delaware, Maryland, and Virginia. The surface is low and sandy, and along the New Jersey coast we find sandy reefs, shoreward from which are lagoons succeeded by extensive areas of swamp. The country is low, nowhere rising above 100 feet above the sea-level.

"THE SOUTH ATLANTIC COAST REGION includes the coast counties of North Carolina, South Carolina, and Georgia, with extensive reefs, inclosing large bays and sounds. A large proportion of the area is low and swampy. The average elevation above the sea is less than 100 feet.

"THE GULF COAST REGION includes the entire State of Florida and the coast counties of Alabama, Mississippi, Louisiana, and Texas. In Florida and Louisiana a large portion is uninhabited swamp land. The elevation is less than 100 feet.

"THE NORTHEASTERN HILLS AND PLATEAUS include all that portion of Maine, New Hampshire, Massachusetts, and Connecticut not comprised in the coast strip, with all of Vermont and the northern portion of New York State, including the Adirondacks. The area is not all, strictly speaking, mountainous It includes a large amount of hills and broken country. It was originally covered with dense forests, which have in the settled portion been cut away. The elevation is mostly above 500 feet, and in considerable parts rises to mountains from 3000 to 6000 feet above the sea.

"THE CENTRAL APPALACHIAN REGION comprises the Catskill region of southeastern New York, the central portion of Pennsylvania, and the western part of Maryland, and chiefly consists of narrow, parallel ridges, with singularly uniform crests, broken by few gaps, and

rising from 1000 to 2000 feet above the narrow valleys separating them, which in their turn are from 500 to 1000 feet above the sea.

"THE NORTHERN LAKE REGION comprises those parts of New York, Ohio, Indiana, Illinois, Michigan, and Wisconsin which border on the great lakes. These large bodies of fresh water exert a considerable influence upon the climate, in moderating the extremes and in rendering the atmosphere humid. The mean elevation is about 300 feet above the sea.

"THE INTERIOR PLATEAU comprises that portion of the plain from the base of the Appalachians eastward, which includes parts of Pennsylvania, Virginia, and North Carolina; and also on the west side of the Appalachians, the plateau country of central New York, and western Pennsylvania. The surface is broken and hilly, but nowhere rises into mountains. It was upland country originally, covered with forests, which have been largely cleared away. It contains comparatively little water surface or swamp land.

"THE SOUTHERN CENTRAL APPALACHIAN REGION includes portions of Virginia, West Virginia, the Carolinas, Kentucky, Tennessee, Georgia, and Alabama. This is largely a mountainous region, 5000 to 6000 feet in height on the north, gradually diminishing in the south to 1000 feet or below. This region is largely covered, especially in the south, with heavy forests of pine and hard wood.

"THE OHIO RIVER BELT includes those parts of Ohio, Indiana, Kentucky, and West Virginia which border on the Ohio River. It is broken country, more and more diversified in the upper part of the river. For the most part the rivers flow in deep, narrow valleys, bordered by high bluffs and broken hills. Elevation, 500 to 1000 feet.

"THE SOUTHERN INTERIOR PLATEAU includes the section of the Atlantic plain which extends across South Carolina, Georgia, with the region in central Alabama and Mississippi lying between the Appalachian region and the Gulf-coast belt. It is mostly level and heavily timbered, principally with pine, a large part of which being what is popularly known as "pine barrens." It is a warm climate, the temperature rising higher than on the coast. Elevation, below 1000 feet.

"THE NORTHERN MISSISSIPPI RIVER BELT extends from the mouth of the Ohio River to the head of the Mississippi River, including portions of Missouri, Iowa, and Minnesota on the western, and of Illinois and Wisconsin on the eastern, bank. Elevation, 500 to 1000 feet

"THE SOUTHWEST CENTRAL REGION includes the northwestern part of Louisiana, the southern part of Missouri, all of Arkansas except that belonging to the south Mississippi River belt and central Texas. It is mainly upland, and, except parts of Texas, is heavily timbered. Elevation, 100 to 500 feet.

"THE PRAIRIE REGION comprises most of the State of Illinois, the southern part of Wisconsin, nearly all of Iowa, southern Minnesota, the northern part of Missouri, the eastern half of Kansas, a considerable portion of Nebraska, and part of Dakota. The surface is nearly level, except where cut by streams. Forests cover but a small portion of the area. The soil is deep, extremely fertile, and generally very retentive of moisture. The elevation is from 500 to 1000 feet on the eastern portion, gradually rising to from 2000 to 3000 feet in the west.

"THE NORTHWESTERN REGION comprises parts of Minnesota, Wisconsin, and Michigan. It is heavily timbered and well watered, containing large numbers of small lakes and considerable areas of swamp. This large water surface, together with dense forests, tends to give this region a moist atmosphere, although the rain-fall is not great. The elevation is from 1000 to 1500 feet.

"THE PACIFIC COAST REGION comprises the coast regions of Washington and Oregon Territories and California lying between the Cascades and Sierra Nevada and the Pacific coast. The surface consists of a complex range of mountains, known as the coast range, running parallel to the coast, east of which is a great valley extending from Puget Sound to the southern part of California. The elevation varies from the coast-line to 8000 feet."

If, now, we examine Table III, we find the highest mortality from diabetes in the United States is reached in the Northeastern Hills and Plateaus. The mean temperature for this region is from 35° to 45° F., and the mean elevation is about 1500 feet,—the coldest and one of the most elevated regions in the country. We therefore find that, whether we take the State as a unit, or a group of States, the territory which furnishes the lowest mean temperature and the highest altitude also furnishes the highest mortality from the disease under consideration. The Pacific Coast Region furnishes the next highest mortality from diabetes of the State groups in the country. The mean temperature of this region is about 55° F., and the average elevation is about 1000 feet. The temperature, as will be observed, is not sufficiently low to explain the very high mortality of the disease in this region, although the altitude is such as

to partly counterbalance the higher temperature. But, comparing both the temperature and altitude of this region with some others,—such, for instance, as the Southern Central Appalachian Region,—we still find the mortality from diabetes in the Pacific Coast Region unduly high. After a careful consideration of all the conditions of this region, I have no doubt that the unduly high mortality from diabetes here is more apparent than real, as it is with other diseases, such as consumption. In other words, the salubrious climate of the Pacific coast attracts many invalids suffering from diabetes, who there die, and thus unduly swell the records.

In the Northwestern Region we note a very high ratio of mortality from the disease. The mean temperature for this region is very low,—about 45° F.,—and the elevation is high—1500 feet.

If, now, we pass to the extreme opposite conditions of temperature and altitude—such as the Gulf Coast and Southern Interior Plateau—where the mean temperature range is from 60° F. to 75° F., and the altitude for the most part is below 100 feet, we find the lowest mortality from diabetes in the country.

The Ohio River Belt, the Northern Mississippi River Belt, and the Prairie Region all furnish comparatively high ratios of mortality from diabetes; their mean temperatures are comparatively low, and their altitudes are comparatively high. Thus, from whatever stand-point we view the subject, we must conclude that, in the United States, diabetes attains its highest mortality in the lowest range of temperature in conjunction with the higher altitudes, and *vice versâ*.

I have thus far said nothing as to the effects of moisture over diabetes, because the evidence upon this point seems rather contradictory. As a rule, the more

humid climates—if we measure the humidity by the mean rain-fall—are those in which the temperature range is the highest; and since, as already shown, the temperature is the strongest determining influence over the mortality ratio, it follows, as a rule, that the lower mortality is attained in the more humid climates, not, however, as a result of the greater humidity, but as a result of the accompanying high temperature. Thus it will be observed, upon examination of Table III, that in the South Atlantic Coast Region and Southern Interior Plateau the mean rain-fall is the highest in the country. These regions, as already noted, furnish the very lowest ratios of mortality from diabetes in the country—.76 and .86 per 1000 deaths. This has already been shown to be due to the high temperature, combined with the low altitude, and therefore not to humidity of the atmosphere. But, notwithstanding all this, I am inclined to believe that a moist atmosphere, even in warm climates, has an appreciably unfavorable influence over diabetes; and that in northern climates it has a still more unfavorable influence. Thus, directly on the Gulf coast the mortality from diabetes is slightly higher than it is a few miles in the interior, and this holds true from Florida to Texas inclusive. In the North Atlantic Coast Region—one of the most humid in the country—although the altitude is low, yet the mortality from diabetes is moderately high—2.91. Again, take the Northwestern Region, where, although the mean rain-fall is not high (30 to 40 inches), yet in consequence of the numerous lakes scattered over the region the atmosphere is moist. The mean temperature is but moderately low, and nearly the whole tract is protected by dense forests, yet the mortality from diabetes is decidedly high—2.74. On the whole, it therefore seems probable that a moist

atmosphere slightly modifies the favorable influence of high temperature over diabetes, and that it emphasizes the pernicious effects of cold over the disease.

From all that has been said, it will be seen that the most favorable location for residence for diabetic patients, in the United States, is within the area of territory bounded on the east and including the South Atlantic coast, and from thence extending westward and including the Southern Interior Plateau and the Southwest Central Region. It includes, in part or in whole, the States of North Carolina, South Carolina, Georgia, Alabama, Mississippi, Louisiana, Arkansas, and Texas. In addition to the climatic advantages of the territory just named, it possesses another,—and one of no mean importance to diabetic patients,—viz., the almost perennial supply of those foods which, as will be later shown, are most suitable to their condition. On the whole, probably no place on the inhabited globe is better suited for a residence for diabetic patients than the belt of country embracing the States above named.

By no means the least interesting feature occurring to me, in the course of these investigations, was the development of the fact that the territories furnishing the highest mortality from diabetes in the United States coincide very closely with those furnishing the highest mortality from consumption. The very frequent termination of diabetes in consumption, as will be shown later on, lends significance to this fact.

The next question claiming attention in the climatology of diabetes is the comparative mortality of the disease in the rural and urban population. Dickinson holds the view that the mortality from diabetes is higher in rural than in urban populations; while Sir William Roberts has arrived at directly the opposite conclusion. Here, again,

our own country offers exceptional facilities for solving climatic features of the disease, which I have endeavored to bring forward. It will be remembered that while the population of Great Britain is about 268 to the square mile, that of the United States averages only about 14. The density of population in our own country is, therefore, such as to render the contrast between urban and rural life much stronger than in Great Britain.

I have in Table IV selected twelve regions of the country, and carefully tabulated the ratio of mortality from diabetes in the rural and urban population in each region. As near as possible I have selected examples of the typical climates of the country, the regions of which at the same time contain sufficient number of large towns and cities to make the contrast between rural and urban life as strong as possible.

TABLE IV.—*Showing Ratio of Death from Diabetes in Rural and Urban Populations in the United States in 1880, by Regions.*

REGIONS.	DEATHS FROM DIABETES PER 1000 DEATHS.	
	Rural.	Urban.
1. North Atlantic Coast Region	3.55	1.76
2. Middle Atlantic Coast Region	1.27	.88
3. South Atlantic Coast Region	.70	1.15
4. Gulf Coast Region	.49	1.56
5. Northeastern Hills and Plateaus	3.98	2.43
6. Central Appalachian Region	2.51	1.35
7. Northern Lake Region	3.47	1.15
8. The Interior Plateau	2.51	1.42
9. The Ohio River Belt	2.96	.82
10. Northern Mississippi River Belt	2.09	1.84
11. Central Regions (Plains)	3.30	.64
12. Pacific Coast Region	2.69	2.53

An examination of Table IV discloses the fact that in the northern regions of the country, such as the

North Atlantic Coast, the Northern Hills and Plateaus, and the Northern Lake Regions, the mortality from diabetes in the rural population greatly exceeds that in the towns and cities,—in fact, it nearly trebles the latter. It is further remarkable that in the Central Region of Plains and Prairies the rural mortality from the disease is more than five times greater than that in the towns and cities. The mean temperature of the latter region is about 55° F., and the elevation is about 1000 feet above the sea. The country for the most part is a level and exposed plain, the little timber which occupied it having been cleared away. The winds are, therefore, unobstructed, and for much of the year are cold and severe. No stronger argument could possibly be brought forward than the conditions in this region, to prove that exposure in northern climates greatly increases the mortality from diabetes in the rural over that in the urban populations. In further examination of Table IV, however, we meet with the curious fact that in the warmer climates the conditions as to mortality are directly reversed. In the South Atlantic and Gulf Coast Regions, the mortality from diabetes in the towns and cities greatly exceeds that in the country,—in fact, it is more than double the latter. It will, therefore, be perceived that the relative mortality of diabetes in rural and urban populations is chiefly determined by temperature, in the colder regions the mortality being decidedly higher in the country, while in the warmer regions it is higher in the cities. The explanation of these facts appears to me to be as follows: Cold, as already shown, greatly increases the mortality from diabetes. In cold climates, those who are best sheltered from exposure suffer least from the disease. This fact is brought out in strong contrast in the United States, because there the houses

are constructed with a view to greater warmth and comfort than in Europe. In the warmer climates of the South the evil effects of cold no longer operate, and the atmospheric conditions affecting the disease are chiefly those of purity. The country people are able to live in the open air the year round without exposure to cold or chill, and oxidation attains its greatest activity. In the cities more or less confinement and impurity of atmosphere is inevitable, which tends to impede oxidation and give greater impetus to the disease.

It is a remarkable fact that the mortality reports of the United States census for 1880 do not furnish a single death from diabetes in either the Indian or Chinese population of the country. With regard to the Indian population this, perhaps, does not seem so surprising, considering the habits of this race as to eating, since, as a rule, they are spare eaters, and subsist almost exclusively upon nitrogenous foods. With regard to the Chinese population, the explanation is by no means so easy. It may be observed, however, that the reports bear out the records from their native land, where, as already stated, we have no reports of the disease. The exemption from the disease enjoyed by the Chinese is, therefore, in all probability due to a race peculiarity.

From a comparison of the mortality records of the four last United States census reports, I have been able to ascertain that the relative mortality from diabetes in this country has been very decidedly on the increase during the last forty years. Thus, the census reports for 1850 give a death-rate from diabetes in the United States of 72 per 100,000 deaths; that for 1860 shows 98 per 100,000 deaths; that for 1870 shows 170 per 100,000 deaths; and that for 1880 shows 191 per 100,000 deaths. It will, therefore, be seen that the death ratio from dia-

betes in the United States has increased 150 per cent. within the forty years ending in 1880.

TABLE V.—*Ratio of Deaths from Diabetes in the United States from 1850 to 1880, Inclusive.*

YEAR.	RATIO.
1850	72 per 100,000 deaths.
1860	98 " " "
1870	170 " " "
1880	191 " " "

It will be observed, upon examination of these records, that the increase of the death ratio from diabetes during the first period of ten years—from 1850 to 1860—was about 30 per cent. Between 1860 and 1870 the death-rate increased to the enormous proportion of nearly 100 per cent. In the last decade, from 1870 to 1880, the rate of increase has only been about 8 per cent. I can assign but one cause for the enormous increase of the death-rate from diabetes during the period from 1860 to 1870, viz., the decided change in the habits of the nation in living, consequent upon the civil war. Previous to 1860, the inhabitants of the United States were a frugal and economical people, enjoying but moderate luxuries in living. With the war of 1860 came inflation of the currency and hitherto unknown abundance of money. The consequence, as is well known, was that the people entered upon a career of luxurious living, which has earned for them the reputation of being the most extravagant nation in the world. It seems altogether probable, therefore, that such marked and sudden changes of life, from those of frugality to luxury, which extended even to the hitherto poorer classes of the people, largely accounts for the decided impetus given to the disease during the period named.

SECTION II.

PHYSIOLOGICAL AND PATHOLOGICAL CONSIDERATIONS.

DIABETES MELLITUS may be defined as a disease characterized by a perverted elaboration in the economy of the food products whereby chiefly, though not exclusively, the carbohydrates become converted into sugar; and the efforts of the system to eliminate the latter give rise to certain symptoms and disturbances which will be described later in detail. Viewed from whatever etiological stand-point we choose,—whether we accept the nervous, the muscular, or the hepatic theory of its origin,—the essential features of the disease consist of a perversion of the elaborating mechanism of the organism. Our present knowledge of physiological chemistry renders it more than probable that this disturbance is chiefly seated in the liver; and for the last fifty years the most earnest efforts have been put forth in attempts to unravel the nature of this morbid process.

Bernard laid the foundation of subsequent research by demonstrating that one of the functions of the liver in health is the formation and storing up of glycogen, or animal dextrine,—a substance chemically identical with starch. Bernard showed that when an animal is recently killed and the liver is removed and placed in a warm place, it soon becomes charged with sugar by the conversion of part of this glycogen into glucose. If next all the sugar be washed out of the liver by means of a stream of water, and the organ be permitted again to remain in a warm place for twenty-four hours, it becomes abundantly charged again with sugar. This may be

repeated again and again until finally all the glycogen contained in the liver is converted into sugar. Since the sugar obtained from glycogen or animal dextrine in the liver is identical in all respects with the glucose found in diabetic urine, it cannot be doubted that the source of diabetic sugar is the liver.

It has just been stated that glycogen is chemically identical with starch. They are both convertible into glucose by contact with saliva, pancreatic juice, or diastase. They possess one important difference, however, viz., glycogen is converted into glucose by contact with arterial blood, while starch remains unchanged by the latter. The blood, therefore, contains a peculiar ferment, capable of converting animal dextrine into sugar; as yet this ferment has not been isolated.

Schiff has shown that this ferment totally disappears from the blood of frogs during the second half of the winter and the early spring months. During this time, although the liver is as full as usual of glycogen, no production of sugar occurs when the liver is isolated; and, moreover, artificial glycosuria cannot be induced in these animals at such times. It is important in this connection to note that animal dextrine, although always present in the livers of all healthy animals, yet under a variety of diseased and unnatural conditions it quickly and entirely disappears. This explains why it is rarely to be found if sought for post-mortem.

Before it be possible to comprehend the part tnat glycogen plays in the production of diabetes, it is first necessary to inquire into its source, formation, and destination in the organism in health. Great divergence of opinion prevails among physiologists upon this question, most of whom, however, at present adhere to one of two theories. Bernard believed that a continual con-

version of this glycogen into sugar is going on in the liver during health, and that sugar is being constantly poured into the portal vein and distributed in the circulation to be consumed in the lungs and muscles. In other words, Bernard's view is that the liver in health is a sugar-forming organ, and that glycosuria only results from failure of the system to appropriate the sugar formed in the liver.

On the other hand, Dr. Pavy holds that in health there is no conversion of glycogen into sugar going on in the liver, nor any stream of sugar flowing into the circulation through the hepatic vein, and that when such does take place it is the result of diseased conditions, similar to diabetes, or the result of post-mortem changes. To use his own words, "Instead of the liver being essentially a sugar-forming, it is a sugar-assimilating organ. Its great function in relation to sugar is to prevent this principle reaching the circulation to any material extent."

The chief evidence in favor of Bernard's theory rests upon his assumption that in recently-killed animals the blood in the hepatic veins contains considerably more sugar than does the blood of other parts of the body. Dr. Pavy considers the results obtained by Bernard's experiments due to rapid changes which occurred during the experiments. He varied these experiments with the view of avoiding these changes, and obtained an altogether different result. By catheterizing the right heart, and introducing a tube along the jugular vein, he was able to obtain the blood of the hepatic veins in its normal condition. Thus obtained, the blood was found to contain only the normal traces of sugar which are common to all parts of the circulation.

With regard to diabetic conditions, Bernard and his

school take the ground that glycogen has its normal seat in some hepatic cells, while the ferment which is capable of converting it into sugar resides in other cells, the union or separation of these two substances being determined by the nervous system. In proof of his position Bernard pointed out that injuries to that part of the medulla which includes the vasomotor centre for the liver—floor of the fourth ventricle and vicinity—produce artificial glycosuria in perfectly healthy animals.

Dr. Pavy admits the nervous influence so far as the production of hyperæmia of the liver through vasomotor paralysis; but he considers the diabetic condition as one of chemico-physiological derangement of the liver. In other words, he considers that the carbohydrates in healthy digestion are changed into maltose, dextrine being an intermediate product. When glucose is ingested it is converted in the stomach and intestines by means of the glucose ferment into maltose, and the maltose, from either source, under the influence of a good venous blood, becomes absorbed and assimilated. In the diabetic condition, in consequence of the vasomotor paralysis, great dilatation of the vessels of the chylopoëtic viscera occurs, and the blood, entering the liver in an imperfectly deoxygenated state, gives rise to a glucose-forming ferment. Since the glucose thus formed is not assimilated, it passes into the circulation and appears in the urine.

Without entering into a minute consideration of the numerous experiments and arguments which have been brought forward in support of either of the above doctrines, it seems to me altogether probable that the explanations of Dr. Pavy, both as to the physiological function of the liver in relation to glucose, as well as

the production of diabetes, is more nearly the correct one.

Our present knowledge strongly indicates the view that the ultimate destination of the carbohydrate foods in the economy is the formation of fats. Now, almost the first step in pronounced diabetes is that of rapid emaciation, without any increase of temperature or loss of appetite; on the contrary, the temperature becomes lower than normal, and the appetite becomes increased. It is evident that the emaciation in diabetes means that the elements which normally go to make up fat do not reach their destination in the economy, but are turned aside during some step in the metamorphosis, and constitute the waste. That this defect occurs in the liver there can be little doubt. If this be the correct explanation of the pathological processes in diabetes it would seem to harmonize best with the varied and uncertain lesions found, the multiple methods by which it may be artificially induced, and the many gradations of its intensity.

If we accept the explanation of Bernard we must assume that considerable quantities of sugar circulate in the normal blood. If we attempt to trace it to its destination in this fluid, we find the theory that it is oxidized in the lungs is an untenable one; for the blood in the right side of the heart is found to contain no more sugar than that in the left side. It has been assumed that in health the sugar is converted in the muscles into lactic acid by means of a ferment, and that lack of this ferment permits the sugar to remain unchanged when it accumulates, and escapes by the urine. Experiments upon animals, however, demonstrate that when they are frozen to death—a process which arrests fermentation—no glycosuria results. In addition to this no antece-

dent changes in the muscular system are present in diabetes that are observable—certainly no grave nutritional alterations, such as must necessarily follow the diversion of so large an amount of the normal pabulum.

It has already been stated that the carbohydrate foods are the chief source of sugar in the economy, but it must not be forgotten that they are not the exclusive source of that product. Dr. Pavy found by experiments upon dogs that, when fed exclusively upon animal food, the average proportion of glycogen in their livers was 7.19 per cent. Upon vegetable food, including potatoes, barley-meal, and bread, the average percentage of glycogen reached 17.23. Dr. McDonald* extended these observations to other animals, and obtained results which show that glycogen reaches its greatest amount under the ingestion of starch and sugar; that it is still formed, though scantily, upon a diet of albumin, fibrin, and glutin; while upon a diet of animal oil or fat, vegetable oil, and gelatin, glycogen almost entirely disappears from the liver. With regard to the formation of sugar upon a purely nitrogenous diet, Professor Houghton has suggested† that the nitrogenous elements may be split up in the liver into glycogen and urea. Albumin closely corresponds chemically to a combination of these two products,—the nitrogen corresponding to the urea, the hydrogen and carbon to the glycogen. It will be observed that in diabetes the sugar and urea in the urine usually increase and diminish together, which strongly indicates their common origin.

We have next to consider the part played by the nervous system in the production of glycosuria. Bernard

* McDonald on Functions of the Liver, p. 14.

† Houghton on Diabetes Mellitus, Dublin Quarterly Jour., November, 1861, p. 269.

demonstrated that puncture of the floor of the fourth ventricle of the brain is immediately followed by glycosuria. It was at first supposed that the glycosuria thus induced was brought about through irritation of the pneumogastric nerves, but subsequent experiments showed that puncture of the medulla caused the urine to become saccharine, even when the vagi were divided. It was further proved that the glycosuric influence was not conveyed from the brain to the liver through the vagi by the following experiments: Without puncture of the medulla, the vagi having been divided, the cut end connected with the liver was subjected to galvanism without inducing glycosuria; when, however, the cerebral end of the nerves were galvanized, glycosuria at once resulted. The vagi, therefore, are capable of conducting the glycosuric irritation to the nerve-centres, but not toward the liver.

It would occupy too much space here to detail the numerous, though interesting, experiments conducted by Schiff, Pavy, Eckhard, Aladoff, and others, with the object of defining the route of the so-called glycosuric influence from the vasomotor centre in the medulla to the liver. It may, however, be stated that, starting with the suggestion of Bernard that the route probably lay along the spinal cord and splanchnic nerves to the liver, experimenters have succeeded in mapping out this course with a reasonable degree of certainty, as follows: Beginning at the glycosuric tract, which, broadly speaking, comprises that part of the cerebro-spinal axis which is included between the optic thalami and the lower end of the cervical enlargement, the glycosuric influence passes into the spinal cord; then by filaments of the sympathetic, which accompany the vertebral artery into the lower cervical ganglion; then through the annulus Vieussens

into the first dorsal ganglion; from thence through the prevertebral cord of the sympathetic and branches to the liver.

Artificial glycosuria may be brought about by numerous traumatisms and influences more or less profoundly affecting this nervous mechanism, by cutting or puncturing various parts of the nerve-centres, or the nerves leading therefrom; by drugs which act powerfully upon the nervous mechanism, either directly upon the vasomotor centre, or indirectly by reflex action through the sympathetic system. Thus, glycosuria has been induced by poisonous doses of strychnia and curare; by inhalations of chloroform and ether; by wounding the liver by means of needles, or injecting acids or stimulants into the hepatic veins; by violently irritating some sensory nerve, and by injecting arterial blood into the portal vein, etc. It is probable that most, if not all, of these injuries act in a similar way,—paradoxical though this may seem,—viz., by irritating the vasomotor centre, either directly or indirectly, resulting in dilatation of the vessels of the liver and consequent hyperæmia of the organ and its attendant glycosuria. Artificial glycosuria, however brought about,—except through lesions of the pancreas,—passes away in a short time, rarely lasting longer than twenty-four hours, and this strongly suggests that the nature of the cause is one of irritation.

On the other hand, in permanent diabetes the condition of the vasomotor apparatus is one of paralysis, and, although our knowledge has not yet reached precise data as to pathological causes, our researches in artificial glycosuria have paved the way to their very threshold.

Finally, in addition to the diabetes of nervous origin, recently-ascertained facts render it strongly probable, if indeed not certain, that diabetes sometimes arises in an

entirely different way, originating, as Lancereaux long ago maintained, from lesions of the pancreas. Von Mering has shown in the most conclusive manner that complete ablation of the pancreas in the dog is followed by more or less intense diabetes, which usually lasts until the death of the animal. Lépine has recently published the results of four such experiments, which are both interesting and instructive. In the first case no diabetes resulted from the experiment, there being peritonitis from perforation caused by gangrene of the duodenum.* The second dog presented no glycosuria during the whole time it lived after the removal of the pancreas; but at the autopsy it was found that part of the pancreas remained. The fragment remaining had no connection with the duodenum. This dog, although he had no glycosuria, yet according to analysis he had hyperglycæmia,—about 2 grammes of sugar per kilogramme of blood. The third dog, after the removal of the pancreas, had no glycosuria during the first three days; then after having been fed there appeared 5 grammes of sugar to the litre of urine. Two hundred grammes of glucose were then administered, and the following day the urine contained 50 grammes of sugar to the litre,—about 25 grains to the ounce. This intense diabetes persisted until the death of the animal. The fourth dog survived twelve days, and during all this time it was diabetic, passing from 40 to 80 grammes of sugar daily. Examination of the blood of this fourth animal showed intense hyperglycæmia, the arterial blood containing 8 grammes of sugar per litre.†

Lépine has suggested two hypotheses in explanation of diabetes of pancreatic origin. The first suggests that

* It will be remembered that febrile and inflammatory processes at once arrest the excretion of sugar in the urine of diabetics.

† Lyon Médicale, December 29, 1889.

in the normal state a part of the pancreatic ferment is re-absorbed and contributes to the destruction of glucose. This is supported by the known action of the diastatic ferment of the pancreas. The second hypothesis suggests that, as is now known, the contact of diastase with starch does not result in the formation of glucose, but of maltose; so the diastatic ferments of the saliva and of the pancreatic juice in contact with glycogen furnish a sugar which is likewise identical with maltose. It thus results that the presence of the pancreatic ferment is necessary to transform glycogen into glucose; and if this ferment be wanting the hepatic sugar will not be normal glucose, but some other form of sugar incapable of appropriation by the system, which is eliminated by the kidneys. Thus, in health, the pancreas and liver are both concerned in the elaboration of normal glucose. Therefore, according to Lépine, "whichever of these hypotheses be accepted, pancreatic diabetes will be the result of the withdrawal of the pancreatic ferment, and diabetes will thus result from a relative reduction of the ferment in relation to the quantity of the carbohydrates to be destroyed."*

The above experiments and suggestions are of undoubted value in furnishing a possible solution of the nature of that form of diabetes which, as will hereafter be shown, so frequently follows upon disease of the pancreas.

In concluding this subject, it may be stated that, while our knowledge at present can scarcely be said to have attained exact data with regard to all the physiological and pathological phenomena of diabetes, the most recent advances upon the subject seem to foreshadow the following conclusions:—

* Therapeutic Gazette, March, 1890, p. 122.

(*a*) That the essential feature of diabetes consists of a more or less profound disturbance of the glycogenic function of the liver.

(*b*) That the chemico-physiological changes in diabetes result in arrest of the elaboration of certain foods in their course toward their ultimate destination in the organism,—probably as fats,—and the intermediate product, passing into the general circulation, escapes from the system, chiefly by way of the kidneys, in the form of sugar.

(*c*) That the disease is accompanied by a hyperæmic condition of the liver, and a more or less engorged state of the chylopoëtic viscera.

(*d*) That recently-ascertained facts indicate that, in addition to the liver, the pancreas also is concerned in the production of sugar in the organism,—or, to speak more accurately, in preventing the production of sugar in the organism,—and consequently diseases of the latter organ are liable to induce diabetes.

(*e*) That diabetes may be brought about by diseases which involve the central ganglia that preside over the vasomotor nerves of the liver, by diseases affecting the peripheral distribution of these nerves, and probably also by disorders involving inhibitory reflex action of the sympathetic nervous system.

SECTION III.

ETIOLOGY.

Predisposing Influences.—The most prominent feature of the disease to be noted in this connection is its strongly-stamped heredity; probably 30 per cent. of the cases may be traced to this source. That the disease is much inclined to run in families must be apparent to all careful observers whose experience has brought them much in contact with it. Numerous and interesting are the instances recorded by various authors, showing its marked family preferences, sometimes extending through several generations. Dr. Ralfe has recorded an instance which came under his observation in which the disease attacked successive members of a family extending over a period of nearly a century, and including four generations. Sir H. Marsh also refers to a family in which he traced the disease through four generations. It is not uncommon to observe periods of culmination of this tendency in certain generations, in which the disease becomes almost a family plague, so many are the members who succumb to it. Sir Wm. Roberts speaks of a family consisting of eight children, every one of whom became diabetic. Dr. Pavy refers to a family of seven, four of whom were diabetic; also to another, in which three brothers became subjects of the disease. Diabetes sometimes maintains this strongly-marked fatality through two or more generations uninterruptedly. One of my recent cases is the seventh subject of diabetes in the same family, all of whom became affected with the disease during two generations. Sometimes the disease, like tuberculosis, shows a marked proclivity for certain

families for a certain period, and then skips a generation, to re-appear after a period of exemption. It is altogether likely that, if a more careful system of interrogating patients were practiced as regards family history, a much higher percentage of hereditary causation would be revealed. In the consultation-room patients are proverbially inclined to present the best side of their family histories. Family tradition, in such matters, is feebly cherished, apparently, and easily slips from the memory. In one of my cases direct inquiry at the first visit failed to elicit any family history of the disease. Subsequent circumstances disclosed the fact that both the father and mother of the patient were diabetic.

Whatever be the determining influences of diabetes, they strongly leave their stamp upon the offspring, as, indeed, do most diseases which involve the integrity of the liver or nervous system. In certain families it is not uncommon to note the effects of transmitted hepatic defect, carrying with it a legacy of gout which the offspring is unable to silence by the most abstemious course of living. So, too, with regard to the nervous system; to record its transmitted defects would entail rewriting a large portion of the literature of the subject, so widely distributed are these influences. It has furthermore seemed to me, indeed, remarkable how frequent are nervous disorders in families of diabetic parentage. In this connection it may be noted that diabetes is alleged to be unusually frequent in the Hebrew race. My own experience confirms this observation to a somewhat remarkable degree. I have, at the present writing, six Jewish patients under treatment for diabetes, and my records show nearly a score of cases of the disease among Hebrews within the past three years. In addition to these, several cases have come within my notice

in the practice of my colleagues within the same period. I can also attest, so far as my own experience is concerned, to the almost universally mild character of diabetes among this people. As a single illustration I would mention the case of a young Hebrew woman, 29 years of age, who has been under my care for the past two years. During all this period the disease has been kept under control by moderate limitations of diet, only occasional traces of sugar having been present in the urine. I have rarely, if ever, met with diabetes in so young a subject, save in the more pronounced form.

I have closely interrogated a number of Hebrew patients with the hope of eliciting a cause especial to this race. The only probable explanation derived from these investigations seems to be connected with habits of overingestion of food. I have been assured, by a highly intelligent Jewish member of the medical profession, that, as a class, Hebrews "are very large eaters." In chronic Bright's disease and gout the subjects, as a rule, are large eaters, and I have assuredly traced glycosuria to the same source, as will be hereafter shown. When diabetes is brought about by habits of excessive eating, I have usually found the disease mild in form and easily controlled. Precisely these conditions obtain in the Hebrew race.

Sex.—Exactly one-third of my recorded cases of diabetes to date have been females and two-thirds males. Of 380 deaths from diabetes reported in the State of Illinois from 1880 to 1888, 131 were females and 249 were males. In 1880 the number of deaths from diabetes in the United States, as shown by the mortality reports of the census, were 1443. Of these, 422 were females and 1021 were males. For the ten years ending in 1870 the deaths from diabetes reported in England and Wales

numbered 6494. Of these, 2223 were females and 4271 were males. It will, therefore, be observed that in England and Wales diabetes is about twice as fatal among males as females; while in the United States the disease is nearly two and one-half times more fatal among males than females.

Age.—Diabetes is infrequent in the two extremes of life. The youngest patient whom I have treated for the disease was 3 years and 4 months old, although a case came within my personal knowledge in which the disease began in infancy and terminated with the life of the patient seven years later. At the other extreme of life I have met with but few cases, the oldest patient I have treated for diabetes being 66. Statistics on a large scale indicate that diabetes, from comparative infrequency in childhood, gradually increases and attains its maximum at about 25 years of age; from thence until about the age of 65 years it maintains a pretty constant uniformity; and after 65 its frequency gradually declines until extreme old age, when it again becomes rare.

Climate.—Up to the present time some difference of opinion has prevailed as to the influence of climate over diabetes; and, indeed, the records of the disease—doubtless very imperfect—from various parts of the world render it somewhat confusing in attempting to draw accurate conclusions, owing to their apparently contradictory character. Thus, in Russia, which possesses a typically cold climate, the disease is said to be rare. On the other hand, in Ceylon, which is almost under the equator, and consequently possessing a typically warm climate, diabetes is said to be quite frequent. Notwithstanding all this, I have endeavored to demonstrate, by a careful consideration of the climatic conditions in the United States, that diabetes, at least in our

country, is directly and decidedly increased by cold and high altitudes, while it is as directly diminished by the opposite conditions. See Section II.

I have had but limited opportunities for studying the influence of climate over diabetes outside of the United States; but if my observations and deductions be correct, there seems no good reason why different results should follow similar conditions of climate in other countries, unless some outside influences prevail which to me are unknown. I strongly suspect, therefore, that, in those countries where the disease is reported as greatly at variance with the climatic conditions which determine its relative frequency in the United States, the apparent discrepancy is due—if the records be not defective—to some other influence than that of climate, such, perhaps, as the life or habits of the people. We have indeed seen, even in the United States, that the race peculiarities of people very profoundly modify the effects of climate over diabetes; for, as was noted in Section I, among the natives of the country,—the Indians,—diabetes is unknown where in the same latitudes in the white population it is frequent. In Ceylon, where, as has been stated, diabetes is frequent, it is certain that the undue frequency is determined by some influence other than climate, for in other climates closely corresponding in most respects with that of Ceylon, such as China, some parts of the African coast, Central America, some of the Pacific Islands, and the West Indies, the disease is rare. The United States combines the largest tract of territory in the world, with the widest range of climate in which the life-habits of the people * are practically identical, and therefore the

* Excluding the relatively small populations of the native Indians and the Chinese.

genuine influence of climate over diabetes, as shown by our mortality records, must be considered as conclusive as are obtainable. It only remains, then, to repeat that which has already been shown in Section I, viz., that cold climates and high altitudes very markedly increase the mortality from diabetes, and *vice versâ.*

Exciting Causes.—When we consider that almost any influence or agency which profoundly disturbs the vaso-motor mechanism of the central nervous system, or very seriously impairs the physiological action of the liver, is capable of bringing about glycosuria, it no longer appears a matter of surprise that the exciting causes of diabetes comprise a wide range of agencies,—so wide, indeed, that it is altogether likely that many remain as yet undetermined.

Mental emotion is undoubtedly the most fruitful exciting cause of the disease. Willis traced the disease to "sadness and long sorrow," and since then numerous observers have recorded cases originating in grief, anger, anxiety, overmental toil, and various forms of mental strain and shock. Rayer mentions a case that followed upon a violent fit of passion. Roberts cites a case which "followed on distress of mind caused by unjust suspicion of theft; in another it followed the burning down of his place of business; in a third it was attributed to anxiety attendant on a Chancery suit."

Dickinson has recorded the case of a woman, who seven months after the death of her husband became diabetic, apparently brought on by inordinate grief. Another, in which "a child fell from a third-floor window, and was smashed upon the pavement to all appearances hopelessly. But the accident was more fatal to its mother than itself. The child survived. The mother never recovered from the shock. For three weeks she

could neither eat nor sleep. Within two months she became much emaciated under diabetes, and died of the disease within ten months of the occurrence upon which it had succeeded."

Dr. Garrod has recorded the following instance: "Two gentlemen fought a duel in Holland; after the first had fired he remained for some time in a state of suspense from his adversary's pistol once or twice missing fire. He was uninjured, but a day or so after became diabetic." In the United States, where commercial competition is very keen, and the possibilities of rapid accumulation of fortune spurs men on to overmental exertion, I am satisfied that diabetes more frequently results than in some of the older communities, where business is conducted under more settled and tranquil conditions, coupled with longer periods of relaxation and rest. Here in the West, where the former conditions prevail so prominently, cases of diabetes very frequently present themselves for treatment from the ranks of the more active business pursuits, which are clearly traceable to the pressure and excitement of business life. As an example, I might mention the case of a bright young man, aged 29, whose diabetes without doubt originated in overanxiety in conducting extensive transactions on the produce exchange. He accumulated a large fortune at the expense of contracting diabetes, which killed him within a year of its onset. In another case, the patient was a man of somewhat large business interests which, becoming complicated, gave him much anxiety and worry. He became very markedly diabetic, and I sent him to the South Atlantic coast for complete rest, where he recovered.

The vasomotor mechanism is, indeed, keenly sensitive to mental influences, and the diabetic condition may be

brought about through this channel in various ways, from too prolonged taxation to the more violent agency of direct shock, or both combined.

Disease and traumatisms of the brain are frequent exciting causes of diabetes, and an almost endless list of examples might be brought forward in illustration. Richardson has recorded a case of diabetes, the autopsy of which revealed an osseous tumor pressing upon the pons Varolii, and an abscess in the posterior cerebral lobes. Dompeling* records a case of diabetes caused undoubtedly by a tumor "as large as a nut," which was found after death occupying the whole right half of the medulla oblongata. Fritz has collected a whole series of cases of diabetes associated with various diseases of the brain and cord. As to traumatisms, blows and falls upon the forehead, vertex, or occiput are the most frequent causes in this class. In the case of the child I have already referred to, the cause seemed to arise from a fall upon the floor of a car, which caused a violent blow upon the occiput. The child became diabetic very soon after, and died of coma within eighteen months.

Fischer has recorded 21 cases of diabetes which were brought about by blows and falls upon the head,—some with and some without cranial fracture. The same observer has recorded over 20 additional cases of diabetes which were brought about by blows on the face, loins, thorax, and abdomen, together with fracture of the vertebra, contusions of the kidney, liver, etc. The disease brought about by these injuries comprises all grades of severity, from slight glycosuria to the most severe type, leading more or less rapidly to death. Freirichs traced 75 of 165 cases of diabetes to some form of nervous lesion, consisting of organic diseases of the brain, mental

* Arch. Gen., May, 1869.

disorders, peripheral nervous disturbances, concussion, blows, and mental strain. In this connection, it may be noted that glycosuria is common in certain types of insanity.

Various other causes are ascribed for diabetes, such as gout, malaria, alcoholism, sexual excesses; and recently Schnée has insisted that inherited syphilis is the most frequent of all causes. I do not agree with the above-named author, since in my experience the effects of inherited syphilis are developed, as a rule, at an earlier period of life than is diabetes.

I have no doubt, as before stated, that overeating frequently induces glycosuria, and in people predisposed to diabetes it sometimes leads to that disease. This result is more likely to follow from overingestion of starchy foods. In such cases the disease seems to be brought about by supernutrition of the portal system.

SECTION IV.

MORBID ANATOMY.

THE liver is frequently found to be enlarged in subjects who have died of diabetes. This change, however, is not a constant one; in fact, some authors deny that it is anything more than an accidental occurrence. More recent and extensive post-mortem researches, however, plainly demonstrate its frequency, if not usual association with the disease. Sometimes the enlargement is slight; at other times it is very marked, the organ reaching two or three times the normal size. With the enlargement the organ is usually darker in color than normal, and somewhat harder in consistence. The essential and most constant changes found are marked dilatation of the hepatic capillaries, hyaline thickening of the walls of the latter, and slight interstitial overgrowth surrounding the hepatic cells, either individually or in clusters, and extending along the walls of the interlobular plexuses. In addition to this, the vessels are distended and enlarged; the liver-cells swollen, somewhat granular, and indistinct in their outlines, with a diminished amount or absence of the normal fat contents.

The lungs exhibit very constant lesions at the autopsy of diabetic patients. These are partly phthisical and partly pneumonic in character,—hepatization, caseation, and excavation being the leading features. It has been questioned by some authors if true tuberculosis of the lungs is associated with diabetes at all; and Dickinson even asserts that diabetic patients enjoy exceptional immunity from that formation. The

cheesy deposits of diabetes mellitus are claimed by this author to differ from those of tuberculosis in the tendency of the former to more rapid excavation, and also to become located in the lower part of the upper lobes, while the tubercular disease nearly always begins at the apex. Notwithstanding all this, with the aid of recent and more exact methods it has been established that, for the most part, these lung-lesions in diabetes are tubercular. Leyden, Rutmeyer, Rugel, and many others have demonstrated the presence of the bacillus of Koch in the expectoration, the pus of the cavities, and the necrotic portions of the lungs in these cases. It may be true that the bacillus tuberculosis is not always found in the sputum in these cases; but the same may be said of tuberculosis in other than diabetic patients. The geographical distribution of diabetes in the United States, as I have already shown in Section I, closely corresponds with the consumption-belt; and the clinical symptoms of tubercular phthisis are practically identical with those of diabetic phthisis, perhaps only modified in the latter case by more pronounced localized pneumonic symptoms. It may be concluded, therefore, that the phthisis of diabetes is identical with tuberculous phthisis, modified, of course, as it must be, by the presence of another disease scarcely less serious than itself.

Besides the cavities found in the lungs in diabetics, the autopsy also reveals the presence of caseous nodules, which are impossible to distinguish by the naked eye from those of tubercular origin. Evidences of circumscribed areas of pneumonia may be noted, such as red and gray hepatization, tending to necrosis and cavity formation.

The pancreas is so frequently found to be the subject of anatomical change in diabetes as to suggest the

probability of causal relationship. In addition to this recent experiments upon animals, consisting of ablation of the pancreas, has been found to be followed almost invariably by diabetes, as was shown in Section II. Senator believes that disease of the pancreas is present in one-half of all cases of diabetes. Lancereaux has reported 14 cases of diabetes associated with lesions of the pancreas. Depierre has recently confirmed these observations of Lancereaux, and cited a number of similar cases. The most common lesions of the pancreas observed at the autopsy in diabetic subjects are fibrosis or hyperplasia of the connective tissue, fatty degeneration of the gland-cells, cancer, calculous concretions in the ducts, with or without obstruction, and in the latter case atrophy or cystic dilatation.

The kidneys are subject to more or less marked anatomical changes, depending chiefly upon the length of time the disease existed before death. The increased demand made upon the kidneys in diabetes, together with the irritating effects of the foreign matter (sugar) which is eliminated in such large quantities, give rise to congestive changes of all grades, from mere hyperæmia up to pronounced swelling and degenerative changes in the excretory structure of the gland. In well-marked cases of diabetes, which have long continued, the autopsy usually discloses considerable enlargement of the kidneys. The surfaces of the organs are smooth, and the capsules non-adherent. The kidneys are overfilled with blood. The tubular epithelium is swollen, granular, and in some cases fatty. Interstitial changes are infrequent unless the disease be associated with Bright's disease. A peculiar "dropsical degeneration" has been described by Cantani, which is confined to the large medullary tubes. The cells become swollen and clear, and almost indistinct.

The heart is the subject of anatomical changes in a considerable percentage of cases,—about 15 per cent., according to recent statistics. Jacques Mayer, whose experience with the disease at Carlsbad has been considerable, has given this subject special attention. In his observations of 380 cases of diabetes, cardiac changes were found in 64 of them. The essential features of the heart-lesions in diabetes, as revealed at the autopsy, seems to be enlargement of the organ without valvular changes. The enlargement is chiefly of the left ventricle, and may consist of thickening of the muscular wall or of dilatation. It has long since been observed that fatty changes in the heart are common in diabetic subjects. Mayer holds the view that the cardiac changes in these cases is due to the irritating effects of sugar and urea in the circulation. Israel has found hypertrophy of the heart in 10 per cent. of the diabetics in the Charité hospital, at Berlin.

In 1885 I published the results of some studies* upon the circulation in diabetes, showing that in a large percentage of the cases there is increased vascular tension, as indicated by the sphygmograph, similar to those in chronic Bright's disease. It would seem that, as in Bright's disease, so in diabetes, an extra demand is made upon the heart, and the regular sequence in all such cases is primarily hypertrophy of the left ventricle, ultimately tending to degenerative changes in the cardiac muscle and dilatation of the ventricle.

The brain, which is believed to be the main-spring of the morbid changes in diabetes, has been most minutely studied by numerous observers in search of anatomical changes which would explain the cause of the disease. Thus far, however, it must be admitted that the results

*Jour. of Am. Med. Association, September 12, 1885.

have been far from uniform or satisfactory. Dickinson, who seems to have been the most industrious investigator in this field, claims that certain minute anatomical changes are characteristic of the disease, although he admits that "the brain of diabetics is almost invariably free from tangible disease, and to rough examination natural." Minute examination, however, he claims, will reveal a fine cribriform or porous condition of the white matter, as if studded with pin-holes, each of the punctures containing a small vessel. The favorite seats of these changes are the corpora striata, optic thalami, pons, medulla, and cerebellum. The fluid in and around the brain is claimed to be slightly in excess, as has been termed a "wet brain"—not uncommon in other conditions. The fluid in the ventricles and beneath the arachnoid is colorless and limpid. A peculiar condition of the spinal cord described, although not claimed to be always present, is dilatation of the central canal, especially in the dorsal and lumbar regions.

These changes are perivascular in nature, and accompanied by minute hæmorrhages or extravasations of blood, apparently occurring rather by transudation than by rupture. These extravasations are said to be most pronounced in connection with the larger perivascular canals, notably between the base and ventricles.

Numerous observers have sought for these changes in connection with diabetes, but without confirming Dr. Dickinson's observations. As Sir William Roberts truly says, "It certainly seems strange, if this wide-spread destruction of nervous matter really occurs in diabetes, that mental aberration and paralytic accidents should usually be so conspicuously absent from the clinical history of idiopathic diabetes." A committee of the London Pathological Society, appointed to investigate

this subject in 1882, reported that they failed to find in the brain "any changes which could be regarded as exclusively or constantly associated with diabetes."

The blood in diabetes, as might be expected, is abnormally charged with sugar, often reaching one-fourth to one-half of 1 per cent. In addition to this, an abnormal amount of fat is present, in some cases sufficient to give the blood a milky appearance. Gamgee has given an analysis of diabetic blood in one case which showed 13 parts of fat in each 1000 parts (the normal being 2).

The blood suffers some impoverishment in diabetes; there is an increase in the proportion of water, and a reduction in the total solids, especially of the corpuscles; and the alkalinity of the blood is markedly diminished.

Such are the chief features of our present knowledge of the morbid anatomy of diabetes. It will be perceived that the disease has not yet given us anything very tangible in explanation of its very remarkable phenomena through the source of pathological anatomy. It has, indeed, been truly said that this "is the most unsatisfactory chapter in our knowledge of the disease." Most, if not all, of the lesions actually present are only found after the disease has been in progress some time, the morbid anatomy of recent diabetes being practically *nil.* These facts strongly suggest that the changes thus far observed are secondary rather than primary, and their nature, for the most part, bears out this suggestion.

SECTION V.

SYMPTOMATOLOGY.

Before entering into a description of the symptoms of diabetes mellitus, it is proper to note that nearly all authors recognize two distinct forms of melituria. First, a milder disorder in which but small quantities of sugar appear in the urine, and these intermittently, the general health of the patient suffering but slight, if any, disturbance; by common consent this form has been termed glycosuria. Second, a more pronounced form of disorder characterized by the excretion of large quantities of excessively saccharine urine, by thirst, morbid appetite, general wasting, and more or less profound disturbance of the general health.

Since glycosuria is a transient condition of no grave import, capable of being brought about by a multitude of agencies, most of which are accidental or artificial, it is of more interest to the experimental physiologist than to the therapeutist. It will, therefore, be chiefly with the second form of the disorder that we shall have to do in the following pages.

By some the second form, or true diabetes, is divided into a mild and severe type, and such division will serve practical purposes if it be not forgotten that these two types may pass indifferently from one to the other in the same subject at any time during the course of the disease.

Thirst, polyuria, lowered temperature, emaciation, and certain nervous disturbances may be considered the classical features of diabetes; but a more minute con-

sideration of these will be greatly facilitated by a systematic review of the effects of the disease upon each of the great divisions of the economy.

The Digestive System.—The effects of diabetes are prominently noted here through more or less pronounced thirst. This, indeed, is often the first symptom to attract the patient's attention; he observes an increased and increasing desire for water. In the mild form of the disease the thirst is not so prominent, and may attract little or no attention, but in the severe type the thirst sometimes becomes enormous, especially in young subjects. I have known a diabetic child to call for water on an average every half-hour, and the amount consumed seemed prodigious. As a rule, diabetic patients will drink from 10 to 12 pints of water daily, but they have been known to drink 30 and even 35 pints per day. Notwithstanding this enormous ingestion of water, the thirst remains unquenched and seemingly unquenchable, for the mouth and throat remain dry and parched. Together with this inordinate thirst, there is usually a morbidly-acute appetite. In the early but well-formed stages of the disease this symptom is specially prominent, the appetite becoming indeed so ravenous that the patient often finds it difficult to satisfy his hunger. As might be expected, the result of such overingestion of food sooner or later tells seriously upon the digestive organs, and, consequently, in the later stages of the disease the patient becomes a prey to various gastro-intestinal disorders. The appetite fails; indeed, often complete anorexia and loathing for all food sets in; gastric pains are likely to follow the latter, becoming more especially prominent upon the approach of a fatal termination. Constipation of the bowels is the general rule throughout, although, in that form of the disease asso-

ciated with pancreatic lesions, an obstinate diarrhœa usually sets in, which baffles the most skillful treatment.

In the more pronounced form of the disease, the mouth, tongue, and fauces present a reddish, congested appearance, not unlike that which is common to inveterate tobacco-smokers. The tongue especially is red and glazed, although sometimes it becomes quite thickly coated with white fur. The whole mouth and throat in severe cases becomes dry, parched, and distressingly uncomfortable. The gums become more or less tender, and their margins frequently become sore and shrink from the teeth, to the extent in some cases that the latter loosen and fall out.

In some cases a more or less constant sweet taste in the mouth is experienced by the patient. This symptom does not seem to bear any relation to the severity of the disease, for in one of my cases the patient was annoyed by it exceedingly when but 1 or 2 grains of sugar to the ounce were present in his urine, and it only disappeared when his urine became non-saccharine. As a rule, the thirst, hunger, and indeed all the digestive disorders become aggravated by the ingestion of starchy and saccharine foods.

The Circulatory System.—In the early course of the disease, the most prominent feature in connection with the circulation seems to be that of lowered bodily temperature. The usual range is 97° F. to 96° F., although it has been known to sink as low as 93° F. Consequent upon this subnormal temperature, the patient is annoyed by more or less chilly feelings, and he instinctively seeks artificial heat by means of extra clothing, or by remaining more than usual indoors. Diabetic patients are proverbially susceptible to colds upon slight exposure, in consequence of their lowered bodily temperature.

Anæmia is not uncommon, especially in advanced stages of the disease, although this is by no means invariably the case. I have elsewhere noted that increased arterial tension, as shown by the sphygmograph, is exceeedingly common in diabetic patients. In pronounced cases I have found this to be the rule, rather than the exception. This is probably in close relationship with cardiac hypertrophy, which is now known to be very frequent in diabetes. Extension of the area of cardiac dullness below and to the left, with accentuation of the second sound of the heart in the second right costo-sternal interspace, and increased tension of the pulse, indicate hypertrophy of the left ventricle, which is frequent in the middle stages of the disease. In late stages the pulse often loses its tension, and evidences of weakened circulation supervene,—such as dropsy and dyspnœa, more or less pronounced. These symptoms are usually associated with fatty changes in the cardiac muscle, with or without dilatation of the ventricle.

The Nervous System.—It is rare to meet with a case of diabetes in which there is not more or less nervous disturbance. Periods of wakefulness are very common, which, unless overcome by the use of narcotics, occasion great loss of sleep. Diabetic patients are usually "nervous" in the popular sense of the term. The more marked the disease, the more pronounced are these symptoms. Neuralgic pains and cutaneous hyperæsthesia are frequent. Sensations of abnormal bodily heat are often complained of. Sudden spells of perspiration are common, sometimes unilateral and sometimes more localized still, affecting only the hands or extremities. The intellectual faculties for the most part remain clear, although as the disease becomes advanced the patient often becomes irritable and fretful, and loses much of

his strength of character. Not infrequently the patient becomes cunning and deceitful in minor matters, especially those relating to his food, resorting to all sorts of ruses to obtain prohibited articles of diet. Finally, as Dr. Dickinson aptly says, "The mind deteriorates morally and intellectually, and the disease, like advancing age, supplies fears to the brave and follies to the wise." The strong, well-balanced mind becomes weak, vascillating, and morose, and the normal equability of temper gives way to frequent spells of irritation, or outbursts of passion. The sexual power deteriorates early in the disease, and later on it becomes abolished,—failure of the power of erection results in complete impotence. Virility may, however, return if the disease passes away. Finally, the late stages of the disease often terminate in gradually-developed stupor, which is followed by profound coma and death. The nature and symptoms of diabetic coma will be fully considered later, under the head of Complications of the Disease, to which it more properly belongs.

The Cutaneous System.—For the most part the skin of diabetic patients is dry, harsh, and unperspirable. The wasting of subcutaneous areolar tissue causes the skin to become wrinkled and loose, which gives the patient, in marked cases, a prematurely-aged appearance. The hands rub together with a harsh, parchment-like sound, and the surface of the skin may often be seen, upon close inspection, to be covered with scurfy-white dust (Pavy).

Itching over the whole cutaneous surface is liable to arise at times, and greatly annoy the patient, especially at night. A case of this kind recently came under my care, which for a time proved very obstinate and rebellious to the usual methods of treatment. More frequent,

however, are the local skin irritations which arise in these cases, especially those at the meatus urinarius in the male, and about the vulva in the female. These distressing local irritations, which may be of all grades of severity, from simple erythema to pronounced eczema, are doubtless caused by the local effects of sugar in the urine, for we find that, wherever the cutaneous surface be bathed with saccharine urine, local irritation ensues. In diabetic children, who are not carefully attended to by the nurse, it is not uncommon to find quite extensive patches of eczema on the inner sides of the thighs and legs, consequent upon the frequent contact of urine with these parts.

Eczema, lichen, and psoriasis are frequent localized accompaniments of diabetes.

The Muscular System.—The chief feature of the disease which claims attention in this connection is wasting. No more constant symptom of diabetes is present than general muscular falling away. In marked cases this wasting is sometimes alarmingly rapid. I have seen patients afflicted with diabetes lose from 40 to 60 pounds in weight within a few weeks. The emaciation usually corresponds with the degree to which the urine becomes saccharine, and is most marked when polyuria and thirst are most prominent. If the excretion of sugar be reduced to the minimum the progressive emaciation becomes stayed, but in pronounced forms of diabetes it is rarely that the loss of flesh can be restored, chiefly because the necessary restrictions of diet do not favor the increase of weight. Occasionally it happens that diabetic patients do not emaciate, notwithstanding very pronounced polyuria and the excretion of large quantities of sugar. Roberts mentions the case of a diabetic who, although he passed 12 pints of highly

saccharine urine daily for some months, still maintained the very generous weight of 210 pounds. A few similar examples have been recorded, but they must be looked upon as exceptional cases.

Muscular cramps are sometimes complained of by these patients, especially in the legs. They are, probably, reflexes from gastric disturbances, as they often are when unassociated with diabetes, and, therefore, they do not merit special attention here.

Aside from the weakness of the muscular system consequent upon the exhausting effects of the disease, I would call especial attention to a peculiar sensation of weariness in the muscles, which I have never failed to observe when the urine is highly saccharine. In practice I often teach my patients the significance of this indication, since it enables them to present themselves for examination upon any return of the urine to a saccharine condition, after a period of exemption from the latter. The urine may be saccharine in some cases without the patient having noticeable thirst or polyuria, but the condition above noted will rarely be absent if the urine be saccharine. This peculiar feeling is one of fatigue, or weariness, rather than actual pain, and it is most prominent in the muscles of the legs and arms. From the fact that this symptom so uniformly appears and disappears with the presence or absence of sugar in the urine, it seems altogether likely that it is due to some deleterious effects of sugar upon the muscular fibres, as it circulates in the blood.

Muscular movements become laborious and fatiguing in pronounced diabetes, and consequently these patients are disinclined to exercise; especially is this the case with regard to active exertion, such as walking.

The Urine.—Very remarkable changes occur in the

urinary secretion in diabetes, both as regards its physical and chemical characters. The physical appearance of the urine is quite characteristic to the practiced eye. It loses its normal depth of yellowness by two or three shades, and becomes of a decidedly greenish hue. When passed in a vessel, it froths much more than does normal urine. It loses none of its normal transparency, but remains perfectly clear in uncomplicated cases. The specific gravity of the urine becomes decidedly increased, and it usually fluctuates between 1030 and 1045, although it may rise to 1074 or sink to 1015. I have usually found, if the specific gravity of diabetic urine habitually sinks much below 1020, that the disease is associated with contracting kidney. The chemical reaction of the urine is usually pronouncedly acid, and it remains so unusually long when exposed to the atmosphere.

The quantity of urine becomes remarkably increased in diabetes, the increase usually keeping pretty accurate pace with the quantity of sugar excreted. Diabetic patients usually void from 6 to 12 pints of urine a day; but in some cases the enormous quantity of 25 and 30 pints have been voided. The daily quantity of the urine varies exceedingly in different cases; it also fluctuates much from time to time in the same case. The chief causes of fluctuation are the character and quantity of food ingested, and the amount of fluids imbibed. It is probable, also, that certain conditions of the system influence the quantity of urine excreted. We know, for instance, that intercurrent febrile conditions cause a decided diminution, both in the quantity of urine and sugar; and they sometimes even cause a temporary disappearance of the latter.

With regard to the chemical changes in the urine in diabetes: The most marked and remarkable of these is

the presence of sugar. The quantity of sugar present ranges from 1 to 8 or 10 per cent., the average in well-marked cases being about 4 or 5 per cent.,—20 to 25 grains per fluidounce. It will be perceived that with the great augmentation of the volume of urine, heavily charged as it is with sugar, a very considerable amount of the latter is eliminated from the system in marked cases. A pound and a half to 2 pounds may be considered the highest daily range in the most severe cases; and from this it may mark all grades in quantity, down to an ounce or less in the milder forms of the disease. As an example of the enormous possibilities of some cases in this direction, Dickinson has recorded the case of one of his patients, who passed 50 ounces of sugar in twenty-four hours, and, he sagely adds, "at which rate he would have made his own weight of sugar within the ecclesiastical period of forty days."

The quantity of sugar in the urine fluctuates considerably during the daily cycle of twenty-four hours, reaching its highest range from three to four hours after meals, and attaining its minimum range during the hours of longest fast—as before breakfast. The quantity sometimes greatly diminishes and, indeed, may disappear upon the approach of a fatal termination of the disease.

The amount of urea in the urine is usually increased in diabetes, the degree of increase corresponding with the severity of the disease. Ordinarily double or treble the normal amount is excreted, but it may reach five or six times more than the healthy standard. It has been claimed that the diet of diabetic patients accounts for the excess of urea in the urine, but this explanation does not accord with facts. The urea maintains even a higher range when the diet is unrestricted than when largely limited to nitrogenous elements; indeed, when

patients are put upon an almost exclusively animal diet, both the sugar and urea in the urine are dminished, not only proportionately, but absolutely. It will usually be found that the greatest excretion of urea corresponds with the degree of rapidity in which emaciation progresses, and this strongly suggests its source, viz., the albuminoids of the system.

Professor Houghton has shown, as already stated, that if albumin be split up its radicals correspond to the sugar and urea, the hydrogen and carbon corresponding to the sugar and the nitrogen to urea, and this is probably the nature of the retrograde metamorphosis going on in the diabetic process. Strong support is lent to this view by the fact already mentioned, that the amount of sugar and urea in the urine increases and decreases simultaneously. Diabetic urine usually contains acetone, or an acetone-yielding substance—aceto-acetic acid. These, probably, do not exist in the urine in a free state, but in combination with some base which is the product of the breaking up of sugar in the blood. Acetone may be recognized by its quality of changing the color of a solution of chloride of iron to a mahogany red. A better test, however, consists of adding a solution of nitro-prusside of sodium and ammonium to the fluid suspected to contain acetone, and, upon shaking well, a rose-violet color is produced, if acetone be present.

The most important morbid chemical product in the urine in diabetes which remains to be considered is the occasional presence of albumin. For the most part, albuminuria is confined to the late stages of the disease, and it is doubtless associated with damage of the kidneys, brought about by long-continued excretion of highly-saccharine urine. The degree of albuminuria is usually slight, rarely exceeding $\frac{1}{4}$ or $\frac{1}{2}$ gramme to the

litre. In cases in which it much exceeds this amount, in all probability some independent renal disease co-exists. Thus, I have seen associated with diabetes a high degree of albuminuria,—4 grammes to the litre,—the origin of the albumin being due to co-existing amyloid disease of the kidneys. When albuminuria arises consequent to, and in the early stages of, diabetes, it is likely to pass away, if the urine becomes permanently free from sugar.

Complications.—One of the most frequent, and certainly the most fatal, of all the complications of diabetes, is a peculiar form of coma—Kussmaul's coma—sometimes termed acetonæmia. Among the younger subjects of the disease this complication is the most frequent cause of death. Few well-marked cases of diabetic coma have thus far been known to recover; the patients usually succumb within two or three days, sometimes even more suddenly.

Two forms of diabetic coma have been described by writers, and, as typical illustrations of each form, I will describe two cases that came under my observation.

In the first case the bowels became constipated for two or three days; the appetite for food almost ceased, and the patient became weak and listless. I was called after these prodromal symptoms, and found the patient complaining much of pain in the stomach and bowels. The respirations were quickened, shallow, and panting, and numbered about 30 per minute. The patient was rather drowsy, and frequently dozed off to sleep in the intervals between the pains. The pulse was small, thready, and increased in frequency to about 100 beats per minute. The patient was seen about eight hours later, when the symptoms were all more pronounced, except the intestinal pain, which was less complained of. The

following day the patient was constantly drowsy, and slept most of the time without narcotics. He could be easily aroused, but lapsed into sleep again in a few seconds if undisturbed. The respirations had increased in number to 40 per minute, and the pulse had risen to 120 beats per minute. In the evening he was found completely comatose; his respirations were 45 per minute; his pulse was 130 per minute, weak, and intermittent. No food had been taken during the day. During the night he sank rapidly, becoming more profoundly comatose, and died before morning—about forty-eight hours after the first alarming symptoms.

In the second case—that of a young woman 23 years of age—after unusual weakness and malaise for two or three days, she was attacked suddenly during the night with severe pain in her stomach, which was followed by vomiting. Succeeding these symptoms was intense gasping dyspnœa, causing the patient to sit up and lean forward, in the typical asthmatic position. She was evidently in great distress, and expressed the fear that she would "choke to death." The pulse became feeble and rapid, the extremities cold; and pronounced symptoms of collapse succeeded, from which, to some extent, she rallied by morning; but in the meantime she gradually became drowsy, with intervals of marked delirium. During the day she became more and more unconscious; the pulse became more feeble and rapid, reaching 150 beats per minute. The respirations were labored and shallow, but not panting or frequent (as in the former case), numbering only 18 or 20 per minute. The patient died in the evening, in a state of coma and collapse.

Other symptoms are not uncommon in diabetic coma, such as a peculiar fruity odor of the breath and urine, the presence of acetone in the urine, and in some cases

tonic convulsions supervene. The chief features of the complication are gastro-intestinal pain, dyspnœa, and more or less rapidly-developed coma and collapse. Diabetic coma may be brought about by fatigue, mental emotion, or some trivial intercurrent illness which under ordinary circumstances would but little disturb the general health. In the case of the young woman just narrated, no especial cause for alarm was present until she contracted epidemic influenza (*la grippe*), which probably precipitated the diabetic coma and caused her death. A highly-acid state of the urine, the presence of acetone in the latter, and constipation of the bowels are usually the preludes to the comatose complication.

As to the cause of diabetic coma: The symptoms certainly indicate that the comatose state is brought about by some toxic agent in the blood, and that this agent is the result of alcholic fermentation of sugar in the blood has thus far been largely accepted as the true explanation. Dr. Ralfe, who has studied this subject closely, holds that the toxic agent is acetone, or an acetone-yielding agent; that when the quantity formed is not excessive, and the kidneys maintain their functional activity, the acetone is eliminated without causing any systemic disturbance; for experiments upon animals prove that considerable quantities of acetone can be ingested without serious consequences. When, however, excessive quantities are liberated in the blood, or when the renal function fails, an excessive quantity is suddenly accumulated in the blood, and then toxic symptoms are at once set up. The frequent appearance of acetone in the urine just previous to the outbreak of diabetic coma, and the persistently diminished alkalinity of the blood in this condition, even when large quantities of alkalies are administered, form the strongest

arguments in favor of the acetone theory of the cause of diabetic coma.

I am inclined to believe, however, that the toxic agent or agents which bring about the coma of diabetes, with its associated phenomena, is nothing more nor less than ptomaines. The extensive retrograde metamorphosis of albuminoid substances constantly going on in high grades of the disease, and the diminished alkalinity of the blood, which entails its diminished oxidizing power, certainly combine the most favorable conditions for originating these toxic agents. In addition to this, the prodromal symptoms of the coma, such as diminution of the urine and constipation of the bowels, by diminishing the avenues of escape, tend to cause accumulation of any toxic agents that may be generated in the system; while some intercurrent disorder or overfatigue, such as usually precedes the attack, disturbs the normal resisting power of the organism to the poison, completes the chain of causative factors, and precipitates the complication, the symptoms of which strongly indicate the nature of the cause.

Pulmonary Complications.—Tubercular phthisis is a very frequent complication of diabetes. It attacks, perhaps, the majority of patients in whom the disease has lasted beyond two or three years. In some respects the symptoms differ from those of ordinary phthisis; the cough is often dry, the expectoration less profuse, hæmoptysis is uncommon, and the temperature is usually below 100° F. Sometimes pneumonia is lighted up in the progress of this complication, or, what is quite as common, the phthisical symptoms begin with bronchitis. The sugar in the urine usually diminishes, and sometimes disappears in the course of the lung complication, probably in consequence of pyrexia, for it

increases and decreases with the rise and fall of the bodily temperature.

Ocular Complications.—Amblyopia is said to occur in about 20 per cent. of the cases of diabetes. Temporary dimness of vision is not uncommon to the disease, and is probably due to defect of adjusting power in the ciliary muscles. More pronounced and often permanent amblyopia is common, and may be brought about by retinal hæmorrhage, atrophy, fatty changes in the retina, or retinitis, and neuro-retinitis; in short, very similar changes to those met with in chronic Bright's disease. These conditions are chiefly met with in chronic cases. The most interesting ocular complication of diabetes, however, as well as one of the most frequent, is that of cataract. Griesinger noted the appearance of cataract in a collection of 225 diabetics twenty times, or nearly one in every 10 cases. It usually affects both eyes, though not always simultaneously, and by preference the right eye first. It may appear without previous defect of vision, or after one or more attacks of amblyopia. Occasionally, it pursues a very rapid course, causing complete loss of vision in one or two weeks. More often, however, it takes several weeks or even months before the vision is destroyed. The cataract is usually of the soft variety, but occasionally it may be firm, especially in aged subjects. Dr. Mitchell has shown that the administration of sugar to frogs causes their lenses to become opaque, the opacity passing away after the animals have been for a time in water. He also found that the lenses could be rendered opaque after removal from the animals by soaking them in syrup. It was thought that these experiments explained the formation of diabetic cataract; but more recent observations have thrown considerable

doubt upon the subject. Hepp has failed to find sugar in the lenses of diabetic patients suffering from cataract. Fischer records similar negative results. In addition to this, diabetic cataract is a permanent condition, and does not improve, even when the urine of the patient ceases to be saccharine, and so remains. Moreover, diabetic cataract nearly always arises in chronic cases, after the disease has lasted two or three years, and this strongly suggests that it is one of the degenerative changes common to the last stages of the disease. As a rule, operations for diabetic cataract are not advisable, for they generally fail owing to almost invariable suppuration of the eye. Wounds in diabetic patients are attended by unusual danger, owing to their proneness to obstinate suppuration, and operations for cataract form no exception to the rule.

Phlegmonous and Gangrenous Processes are frequently the result of diabetic conditions. Perhaps the most frequent of these are multiple boils, which sometimes occur in sufficient numbers to cover the whole surface of the back and shoulders, and even to extend over the extremities. They may be small and confluent, or they may be large and scattered, but in all cases they are phlegmonous and obstinate in their course, often lasting for months by successions of new crops. Prout went so far as to assert that "carbuncles, and malignant boils and abscesses allied to carbuncles," were always accompanied by sugar in the urine. In diabetic conditions they certainly hold some relationship to sugar in the organism, since the surest way of relief from them is to eliminate the sugar from the urine. Max Schuller, who has studied this subject, concludes that they are not due to the specific action of sugar upon the tissues, but are caused by infection, as are other phlegmons.

He thinks it is not even probable that they are due to any special micro-organism peculiar to diabetes, since he has found in them only the round diplococci and streptococci found in ordinary phlegmonous suppurations. We may, perhaps, infer that the presence of sugar in the circulation lessens the resisting power of the tissues to the micro-organisms of phlegmonous suppuration, probably through nutritional changes which it brings about.

Gangrene is an undoubted though not very frequent complication of diabetes. From its preference for the lower extremities, beginning usually in the great toe, as well as from its slow course, it has been described as allied to gangrene of old age. The character and course of the process are largely modified by the nature of the tissues attacked. Dr. Hunt, of Philadelphia, has studied this subject closely, and reviewed 64 cases. He records the locations attacked as follows: The leg below the knee, including the foot, 37; the thigh and buttock, 2; nucha (not ordinary carbuncle), 1; external genitals in females, 1; lungs, 3; fingers, 3; back, 1; eyes, 1. As to the nature of the process, he concludes that "when the tissues are succulent the gangrene will also be of that character; when they are composed mostly of skin, tendon, and bone, they will approach the senile gangrenes in appearance." It is also claimed that diabetic gangrene "never presents the clear-cut line of demarcation between the dead and living parts that is characteristic of the senile variety, and, moreover, there is a lack in the diabetic form of the decided dryness and shrinking of the senile gangrene." Like most complications of diabetes, gangrene is a late accompaniment of the disease.

Albuminuria must be considered a frequent complication of the late stages of diabetes; in fact, it is the

rule, rather than the exception. If the patient be under 40 years of age, the albuminuria is usually unaccompanied by primary lesions of the kidneys, and, as a rule, need not excite any special alarm. The kidneys, in such cases, are doubtless considerably congested, and in some cases enlarged, with slight tubular changes in progress. It is rare, however, for nephritis to assume a sufficiently acute form in these cases to threaten the life of the patient, or to outrun the primary disease. The amount of albumin in the urine is usually small,—½ gramme or less to the litre.

In patients beyond middle age, however, especially those who are well nourished and have been large eaters, if albuminuria be present, it is well to bear in mind the fact that granular atrophy of the kidneys—interstitial nephritis—is frequent, under such circumstances. Such patients will usually be found to have hypertrophy of the left heart; abnormal tension in their arteries; while the urine will usually be found of low specific gravity, containing a small percentage of albumin; and a few perfectly-clear hyaline casts may usually be found, if the urinary sediment be carefully collected and placed under the microscope.

The following illustration from my records of practice will, perhaps, emphasize the practical importance of being on the alert in such cases. Three years ago a gentleman from an adjoining State came to consult me in reference to sugar in his urine, which he said he discovered a year or so before. His "age was 58 years; he had been a 'generous liver,' always had a good appetite, and he was well nourished; in fact, robust. Analysis of his urine showed it to contain 8 grains of sugar to the ounce, and a mere trace of albumin. He was given some directions as to diet, which related more to his

diabetic condition than to his albuminuria. Three months after I was summoned to his home, to find him in the last stage of uræmia, which terminated in death four hours after my arrival." As the sequel showed, his greater danger lurked beneath a faint degree of albuminuria, the result of contracting kidneys; while his greatest fears were aroused by a mild and—in men of his age—comparatively harmless form of diabetes.

It is in such cases that a low specific gravity of urine is sometimes met with. The cirrhotic kidney is unable to excrete the normal amount of solids, and the polyuria still further lowers the proportion of the latter, so that considerable sugar may be present while the specific gravity of the urine remains low,—a seeming paradox in true diabetic conditions. *Amyloid* degeneration of the kidney occasionally complicates diabetes, though rather by accident than otherwise. A chronic necrosis or suppurative process may be in progress, and the system may withstand the drain for months or years until diabetes sets in, which further impairs nutrition and precipitates the amyloid disease. An illustration will be found among the clinical cases in Section VII of this volume.* When amyloid disease of the kidneys complicates diabetes, the urine becomes highly albuminous—2 to 6 grammes to the litre; digestive disorders and diarrhœa follow, and the patient becomes decidedly dropsical.

Course and Duration of the Disease.—In most cases diabetes begins gradually, if, indeed, not insidiously, and it may exist in a latent form for some time. Sooner or later, however, unusual thirst or weakness, and, perhaps, increasing desire to urinate arouses the suspicions of the patient to the fact that he is not well.

* Case 102, J. W., Section VII.

An increased appetite, however, frequently lulls his suspicions, and he may continue for some weeks in the belief that with good digestion he must obviously be all right. His increased appetite, however, but quickens the pace of his disease, by causing an increased ingestion of sugar-forming foods. Increasing thirst, more frequent calls to urinate, and advancing weakness compel him at length to seek advice, which leads to the discovery of his true condition.

Sometimes the disease begins much more abruptly, so much so that the patient is able to fix upon the very day in which it began. His thirst and polyuria make such frequent demands upon his time and attention that it is impossible to overlook them.

The disease may assume still another form of onset, in which nearly all the symptoms remain latent for a lengthy period of time. Slight traces of sugar in the urine may constitute all that is discoverable to indicate any abnormal condition; thirst, polyuria, and wasting being absent. In elderly people especially, the disease often thus begins and continues for a year or more.

The course of the disease, after it has become fully developed, depends upon several circumstances, such as the age of the patient and the character of the treatment employed. *In young subjects the disease is usually progressive toward a fatal termination;* and the younger the patient, the more certain does this hold true. In patients under 30 years of age the disease usually advances with a steady and decided march in its most pronounced form. The thirst and polyuria are prominent; weakness and emaciation become more and more pronounced; the appetite fails; and the patient, in his reduced state, becomes a prey to various nervous disturbances, especially that of insomnia. Dropsy may or

may not appear near the end; but finally one or more of the complications already described—usually coma—closes the struggle, the patient rarely succumbing to the direct prostrating effects of the disease.

If judicious treatment be employed, the symptoms may be considerably modified. Thus the thirst and polyuria may be largely controlled, and even the quantity of sugar in the urine may be reduced to 1 or 2 per cent. But in this especial class of cases, notwithstanding these indications of apparent improvement, the increased emaciation points to the progressive character of the disease. However favorable the aspect of the disease at times may appear, these patients can rarely be made to increase in weight to any material degree; and sooner or later some intercurrent disorder disturbs the balance of resistance, and the disease redoubles its force and carries the patient farther from the line of health. A chance exposure lights up an intractable bronchitis, or a localized pneumonia may be the result, to which phthisis may soon after form the sequel. A score or more of disorders apparently lie in wait for the young diabetic patient, while rarely does the avenue to recovery cross his course. The result, consequently, however long delayed, is pretty surely a fatal one.

Sometimes, as Dr. Pavy has pointed out, the disease advances by a succession of short bounds or leaps, the treatment seeming at times to check its progress; but relapse after relapse at length bring the patient to a condition of extreme marasmus, ending in death.

The disease sometimes pursues still another course; beginning with the most pronounced and even violent symptoms, and after thus continuing for a few weeks, it suddenly assumes a milder form, and so remains, or even passes away. As an illustration of this form of

the disease, a lady from St. Louis two years ago placed herself under my care, who had for six weeks suffered from the usual symptoms of the disease in the most severe form. She had lost 40 pounds in weight within the time above named. She was put upon treatment—chiefly dietetic—and soon her urine ceased to be saccharine, and so far as I know it has so remained. She had regained much of her lost weight before passing from my immediate observation.

The course of diabetes in patients beyond middle age is more variable; but on the whole its progress is more tardy and its symptoms are much less violent. It is not uncommon, indeed, for elderly people to have sugar in their urine almost constantly, without suffering from any marked or disturbing symptoms whatever. Neither thirst, polyuria, nor wasting are present, and the patients are in no way incapacitated for their usual business and social duties. In other cases the disease, while naturally more pronounced, yet a few restrictions of diet hold it well under control, and the patients, by following a few rules as to eating, continue without discomfort from the disease for years, without any apparent progress of the latter.

Exceptionally, even in those well on in years, the disease assumes the more severe type common to youth, as in the case of a woman at present under my care (Case 185, Section VII). The patient, although 50 years of age, suffers from diabetes in its decided and progressive form, notwithstanding the most careful observance of all details of well-directed treatment.

With reference to the duration of the disease, it may be stated that diabetes is essentially a chronic affection, and its course is marked by a compass of years rather than by that of weeks. It is true that occasionally the

disease quickly proves fatal. Dr. Roberts has recorded a case which succumbed in nine days; but such instances are very exceptional.

In younger subjects the usual duration of diabetes is from one to three years, the largest number of deaths recorded being those in the second year. It is not uncommon to meet with cases, in subjects beyond middle age, which survive from five to ten years. Finally, it must not be overlooked that cases are on record in which the urine has been continuously saccharine for over twenty years.

Owing to the somewhat irregular course of diabetes and its susceptibility to modification by treatment, it is impossible to assign a definite duration to any given case.

Diagnosis, including Examination of Urine.—The diagnosis of diabetes presents no difficulties, if attention be directed to the urine. In typical cases, it is almost impossible for the physician either to overlook the disease or to confound it with other conditions. Thirst, dryness, of the mouth, polyuria, muscular weakness, and emaciation are likely to lead to an examination of the urine and the discovery of sugar. It is necessary, as a matter of accuracy, to observe the case for some time, in order to ascertain if sugar be constantly or only occasionally present in the urine,—thus to distinguish between diabetes and glycosuria. In less pronounced forms of the disease, the presence of sugar in the urine may be overlooked, owing to absence of such symptoms as are likely to lead to an examination of the latter. The more routine practice of urinalysis now in vogue renders this error less common than heretofore; especially is this the case in hospital practice.

As the diagnosis of diabetes hinges so largely upon

the examination of the urine, I will briefly review the most practical features of testing the urine for sugar which will best serve the convenience of the general practitioner, without an attempt to include all the tests for sugar which have been brought forward from time to time, many of which I have found too complicated and unsatisfactory for routine work.

Among the numerous qualitative tests for sugar in the urine which have been brought forward to date, the most popular, perhaps, has been that form of the copper test known as Fehling's solution. The original formula for this solution is as follows: Dissolve 34.639 grammes of sulphate of copper in 200 grammes of distilled water; 173 grammes of pure crystallized neutral sodic tartrate are dissolved in 500 or 600 grammes solution of caustic soda (specific gravity 1.12), and into this basic solution the copper solution is poured, a little at a time. The clear, mixed fluid is diluted to one litre. The above solution is very unstable, so much so that it must be freshly prepared in order to be depended upon. With the view of rendering Fehling's solution more stable, Schmiedeburg proposed substituting mannite for the sodic tartrate, which I have found to answer the purpose very well. The formula for the preparation of Fehling's solution, improved as I am in the habit of using it, is as follows: 34.639 grammes of pure copper sulphate are dissolved in 200 grammes of distilled water, to which are added 15 grammes of pure mannite; 500 or 600 grammes of solution of caustic soda are added to the first solution, little by little; finally the whole is brought with distilled water to the volume of 1 litre.

In applying this test, 1 drachm should be diluted with an equal bulk of distilled water in a test-tube, and gently boiled for a few seconds. If it remain clear, add the

suspected urine, drop by drop, and if sugar be present the first few drops will usually cause a yellow precipitate. If no precipitate occur, continue dropping until 1 drachm—not more—of urine be added, re-applying the heat occasionally. If no precipitate occur, sugar is—clinically speaking—absent.

As above prepared, Fehling's solution is entirely stable, and will keep indefinitely. One drachm of the solution responds to $\frac{1}{60}$ to $\frac{1}{100}$ grain of sugar.

Prof. Haines's Test.—On the whole, the most satisfactory qualitative test for sugar in the urine, in my experience, is that prepared after the formula devised by Prof. Walter S. Haines, of Chicago. Its construction is very simple, as follows: Take of pure sulphate of copper, 30 grains; pure water, $\frac{1}{2}$ fluidounce; make a perfect solution, and add pure glycerin, $\frac{1}{2}$ ounce; mix thoroughly, and add 5 ounces of liquor potassæ. A perfectly-clear, transparent, dark-blue liquid results, which, being perfectly stable, may be set aside indefinitely for use. In testing with this solution, take about 1 fluidrachm of the test, and gently boil, when no change should take place; now add 6 or 8 drops—not more—of the suspected urine, and again boil. If sugar be present, an abundant yellow or yellowish-red precipitate is thrown down; if no such precipitate appear, sugar is absent. The white, flocculent deposit thrown down, when non-saccharine urine is added, consists of the phosphates of calcium and magnesium of the urine, which the alkaline character of the test-liquid has precipitated, and it should not be mistaken for an indication of the presence of sugar.

The above test has given me most satisfactory qualitative results in daily work during a continued use of six years. By comparative experimentation I find that

1 drachm of Professor Haines's test responds to $\frac{1}{240}$ grain of grape-sugar.

It is well to bear in mind the fact that the copper tests are liable occasionally—though in reality very rarely—to lead to erroneous conclusions as to the presence of sugar in the urine. Certain normal constituents of the urine—notably uric acid, urates, creatinin, mucus, and pyrocatechin; as well as certain occasional constituents, as oxybutyric acid, urochloralic acid, uroleucic acid, and uroxanthic acid; as well as such drugs as tannin, morphine, salicylic acid, carbolic acid, cubebs, etc.—possess more or less reducing power over the copper tests. The *normal elements* of the urine possess, for the most part, but feeble reducing powers over these tests, and therefore the errors spoken of are actually encountered but rarely. Nevertheless, since such errors are possible, it is well, in cases of doubt, to appeal to such methods as may be considered absolute. Fortunately, we have, in the phenylhydrazin test, introduced by Fischer, one that is entitled to be considered positive in its capability of detecting sugar.

The Phenylhydrazin Test.—This is best conducted as follows: First, introduce in the bottom of an ordinary test-tube a layer of phenylhydrazin—say $\frac{1}{3}$ to $\frac{1}{2}$ inch in thickness; upon this place another $\frac{1}{3}$ to $\frac{1}{2}$ inch of pulverized sodium acetate; next, add water to one-fourth the capacity of the tube; and, lastly, add sufficient of the suspected urine to half-fill the test-tube. Gradually bring the whole to the boiling-point, and boil for about one minute, and then decant into a conical glass vessel, and set aside to cool. In from three to twelve hours take up a few drops of the sediment from the bottom of the glass vessel with a pipette, and place them under a microscope. If sugar be present in the

urine, very peculiar, yellow, acicular crystals will be readily seen—*phenylglucosazone*—which are altogether characteristic. They have a marked tendency to crystallize in stellate or rosette form, or in bundles, like sheaves of wheat.

The *phenylglucosazone* crystals may frequently be seen in half an hour after the boiling; but if none are found after the test has stood twelve hours it may be confidently stated that the urine is free from sugar.

So far as at present known, this test reacts only with *glucose*, *maltose*, and *lactose*.

The above tests leave little, if anything, to be desired in the way of qualitative analysis of urine for sugar. Having once determined the presence of sugar in the urine, it becomes all-important to know, with some degree of accuracy, the quantity thereof, in order to be able to estimate the degree of severity of the disease, as well as to gain some knowledge of its course from day to day.

Now, most of the quantitative tests for sugar in the urine, if, indeed, not all of them brought forward to date, are either complicated, time-consuming, unstable, or inaccurate, and therefore far from satisfactory for practical purposes. The fermentation-test of Roberts requires twenty-four hours' time to reach results which are by no means accurate when obtained. Fehling's solution, perhaps the one most generally depended upon, has been by no means satisfactory in my hands. In view of these facts, I have constructed a formula for a solution which, I trust, will prove as satisfactory in general practice as it has in my laboratory work, where it has answered all that could be desired.

The Author's Quantitative Method.—The formula for this test is as follows:—

℞	Cupric sulphate (pure), . . .	4.15 grammes.
	Caustic potash, " . . .	20.4 "
	Strong ammonia (sp. gr. 0.9), . .	350 c.cm.
	Pure glycerin, ...	50 "
	Aquæ destill., ...	ad 1 litre.

The solution is prepared by dissolving the copper sulphate in part of the water and adding the glycerin. In another portion of the water dissove the caustic potash. Mix the two solutions and add the ammonia. Finally with distilled water bring the volume of the whole to 1 litre and filter.

If it be desired to use the English weights and measures in preparing this test, the formula is as follows:—

℞	Pure sulphate of copper, . . .	½ drachm.
	Caustic potash (pure), ...	2½ drachms.
	Strong ammonia, ...	5½ fld. ounces.
	Pure glycerin, ...	6 fld. drachms.
	Distilled water, . . .	to 1 pint.

The principle upon which the application of this test depends is the fact that a definite quantity of the solution is reduced upon boiling with a definite quantity of grape-sugar, causing the complete disappearance of the beautiful blue color, and leaving a perfectly clear and colorless fluid as the result. Thus, 30 cubic centimetres of this solution are reduced, upon boiling, by ¼ grain of grape-sugar.

The test should be applied as follows: Into a 4-ounce glass flask pour 30 cubic centimetres (about f℥j) of the test-solution, to which should be added an equal volume of *distilled* or *soft water*, and bring the whole to the boiling-point over a spirit-lamp. A pipette, graduated in minims and holding not less than ½ drachm, is now filled with the saccharine urine to be tested, and while the solution is boiling the urine is slowly discharged from the pipette, drop by drop, into the test-

solution, until the blue color completely vanishes and leaves the solution perfectly colorless and clear. The number of minims it takes to discharge the blue color of the solution contain just ¼ grain of sugar. By multiplying this number of minims until the product is 480, the multiple thereof represents the number of quarter-grains of sugar to the ounce, which, if divided by four, gives the number of grains of sugar in each ounce of the urine tested.

The accuracy of this test may be readily proved as follows: Bring 30 cubic centimetres of the solution, in an equal volume of distilled water, to the boiling-point in a glass flask. Then fill the pipette with a solution of grape-sugar of known strength in water (better still, in urine),—say 8 grains to the ounce,—and, as the test-solution is boiling, discharge the sugar solution from the pipette into the boiling fluid, drop by drop, when it will be seen that exactly 15 minims of the sugar solution (or urine) completely discharges the blue color: therefore, 15 minims of the solution contained ¼ grain of sugar, —the exact proportion of a solution of the strength of 8 grains to the ounce.

In testing, the solution should be raised to the boiling-point, and kept slowly boiling; and the urine to be tested should be slowly discharged from the pipette, two or three seconds elapsing after each drop, until the blue color begins to fade; then the drops should be added still more slowly, about ten or twelve seconds elapsing after each drop. By this means the precise quantity of urine may be determined which completely eliminates the blue color of the test-solution, and the most accurate results are obtained.

It may be noted after testing, that, upon cooling, the test-solution slowly resumes its blue color, owing to

absorption of oxygen from the atmosphere and reforming the blue protoxide of copper from the suboxide held in solution by the ammonia.

By means of the above test the quantity of sugar in a given sample of urine may be determined accurately within five minutes; the solution is entirely stable and will keep indefinitely; it is perfectly cleanly and simple in application; no copper products cling to the utensils or obscure the chemical reactions from view.*

Finally, this solution may be used in an ordinary test-tube, and remarkably accurate results obtained by attention to the following details: Measure accurately 1 drachm of the test-solution in an ordinary test-tube and raise it to the boiling-point over a spirit-lamp. Dilute the urine to be tested with an equal volume of water. With a minim pipette, or one the point of which is sufficiently large to drop minims, discharge the *diluted urine*, drop by drop, into the boiling test-solution until the blue color is completely discharged. If 1 minim of the diluted urine discharges the blue color of the test, the urine contains 30 grains of sugar to the ounce, or over. If it requires 2 drops to discharge the blue color, the urine contains between 15 and 30 grains to the ounce. If it takes 3 drops to eliminate the blue, there are between 10 and 15 grains of sugar to the ounce. If it requires 4 drops of the diluted urine to reduce the blue color, there are between $7\frac{1}{2}$ and 10 grains of sugar to the ounce. If 5 drops, there are between 6 and $7\frac{1}{2}$ grains to the ounce. If 6 drops are required, there are from 5 to 6 grains to the ounce. If 8 drops are required, there are from 4 to 5 grains to

* All the copper tests here described are prepared for me and kept in stock by Messrs. Gale & Blocki, 44 and 46 Monroe Street, from whom they may be procured at any time.

the ounce. If 10 drops are required, there are from 3 to 4 grains to the ounce. If 15 drops are required, the urine contains from 2 to 3 grains to the ounce; but if the blue color fails to yield to 15 minims, the urine contains less than 2 grains of sugar to the ounce. Thus, the relations may be seen at a glance by the table below:—

One Drachm of Test-solution.

If reduced by 1 minim of diluted urine, it contains over 30 grains to 1 ounce.

If reduced by 2 minims of diluted urine, it contains between 15 and 30 grains to 1 ounce.

If reduced by 3 minims of diluted urine, it contains between 10 and 15 grains to 1 ounce.

If reduced by 4 minims of diluted urine, it contains between 7½ and 10 grains to 1 ounce.

If reduced by 5 minims of diluted urine, it contains between 6 and 7½ grains to 1 ounce.

If reduced by 6 minims of diluted urine, it contains between 5 and 6 grains to 1 ounce.

If reduced by 8 minims of diluted urine, it contains between 4 and 5 grains to 1 ounce.

If reduced by 10 minims of diluted urine, it contains between 3 and 4 grains to 1 ounce.

If reduced by 15 minims of diluted urine, it contains between 2 and 3 grains to 1 ounce.

In making the above approximate analysis, the first 5 drops of urine should be slowly added, about five seconds elapsing after each drop, during which the solution should be gently boiled; after 5 or 6 drops have been added, the solution may be kept slowly boiling and the urine added, drop by drop, continuously, *but slowly*, until the blue color completely fades, or till 15 minims of the diluted urine be added.

The above tests seem to me all that are required for practical purposes. Those who desire to make themselves acquainted with the other tests for sugar in the

urine which have been brought forward are referred to Dr. Tyson's excellent little hand-book on "Practical Examination of Urine."

If, then, upon chemical examination of the urine as described, it be found that sugar is present to the extent of 5 to 10 or more grains to the ounce, it is strongly probable that the case is one of diabetes; if repeated examinations be made, extending over some time, with the same result, the probability becomes a certainty, and the diagnosis of diabetes mellitus is complete.

Prognosis.—The prognosis in a given case of diabetes depends upon a number of circumstances, the most important of which, perhaps, is the age of the patient. Under 20 years of age the disease is very fatal; indeed, under such circumstances few recoveries are recorded. From 20 to 45 years of age the outlook is more hopeful, the disease being somewhat more amenable to treatment. At the same time, it must not be overlooked that up to 45 years of age diabetes is a very fatal disease, and causes the death of the majority of those who become the subjects of it.

After middle age—say, after 50—the outlook is decidedly more favorable, as the disease then, for the most part, assumes a mild course, and not unfrequently terminates in recovery.

It may be laid down as a general rule that the danger to life from diabetes is in inverse ratio to the age of the patient, thus forming a prominent exception to the usual rule of increasing mortality with increasing age, which is the sequence in most diseases.

The cause of the disease influences the prognosis. Thus, cases traceable to mental anxiety and overmental toil are of more hopeful outlook, especially if the cause be removable. When the disease arises from trauma-

tisms the prognosis is generally more favorable. On the other hand, as Lancereaux has pointed out, when the disease is traceable to diseases of the pancreas, the prognosis is especially gloomy. The length of time the disease has been in progress and the urgency of the symptoms have an important bearing on the prognosis. Cases in which the disease has become confirmed and the emaciation pronounced give little encouragement or hope for the future. On the other hand, if the disease be discovered early, and but little inroads have been made upon the flesh and strength, the general prognosis is always more hopeful.

It is a somewhat remarkable fact, as bearing on the prognosis, that diabetes in stout people is much less serious than in spare people. The development of cataract is usually regarded as very unfavorable in these cases, indicating an early fatal termination. Such cases are said to usually end in death within from six to twelve months; and, although some of them may survive longer, they may be considered as essentially incurable cases. Finally, absence of the patellar reflexes is believed to prevail only in unfavorable cases.

Complications of the disease and intercurrent conditions always render the prognosis grave, and this applies to the most trivial maladies as well as to the more serious. Thus, it is not uncommon for some slight ailment, such as a cold or diarrhœa, to precipitate the more serious features of the disease which before gave no occasion for immediate alarm. Such complications as gangrene, pulmonary tuberculosis, and especially diabetic coma render the prognosis at once unfavorable.

Lastly, the results of treatment enable one, in a measure, to estimate the gravity of the case. Thus, if

the urine become free from sugar upon a restricted diet, we are justified in forming a favorable prognosis; while, if the disease fail to yield to strict dietary measures, and the urine continues heavily laden with sugar, the outlook must be considered unfavorable.

SECTION VI.

TREATMENT.

Prophylactic measures are advisable for people of diabetic parentage, or for those whose families present marked tendencies to the disease. In such cases it is wise to adopt a system of diet which limits the use of starchy and saccharine foods to the most moderate proportions. Occupations should be selected which entail the least possible mental pressure and excitement; and, if practicable, a residence should be chosen as near the sea-level as possible, with a mean temperature range of about 70° F. The observance of the above conditions will insure the individual the best chances of avoiding the disease.

The treatment of diabetes proper may be most systematically considered under three divisions,—dietetic, medicinal, and hygienic.

General Dietetic Considerations.—Until future investigation shall have revealed some agency through which we are able to check the excessive formation of sugar in the liver, our chief resource against the disease must consist in withholding from the system that which it is capable of converting into sugar, and in supplying that which it is capable of assimilating as nourishment. The accomplishment of this object is the essential aim of the dietetic treatment of diabetes.

Physiological chemistry as well as experience have shown us that the chief source of sugar-production in the system is the carbohydrate foods, more especially starches and sugar. In nearly all mild cases of diabetes,

and in most cases of recent origin, the avoidance of these foods arrests the excretion of sugar, as well as the more prominent symptoms of the disease.

It has just been stated that the *chief* source of sugar in the organism is the carbohydrate foods; but, unfortunately, while they are the chief, they are not always the only, source. Experimental investigation has shown that when animals are fed upon purely nitrogenous foods —even for lengthy periods of time—a small amount of glycogen still continues to be present in their livers. In the graver forms of diabetes the "sugar-forming vice" of the organism becomes so strong that the liver is capable of splitting up a portion of the nitrogenous foods, and probably even the albuminoids of the tissues, and of transforming a part of these into sugar. In such cases, while the dietetic treatment is able to modify the excretion of sugar, as well as most of the symptoms, it is not able to entirely arrest the progress of the disease. Fortunately, such cases form a minority of those who become subjects of the disease, and are in nearly all cases very young people, or long-neglected and advanced cases.

The sugar-forming powers of the organism in diabetes are feeblest in their operation upon nitrogenous materials, and therefore animal foods are the least susceptible of conversion into sugar. Next in order rank the green parts of certain vegetables, which quite strongly resist sugar transformation. Finally, the starchy and saccharine members of the carbohydrate group are the most easily transformed into sugar of all, and are therefore the most dangerous for use. Practically, then, the more completely we are able to eliminate the starchy and saccharine foods from the diet, the more completely we are able to hold the disease under control. At first

sight this might seem to be a very simple matter; but when we come to furnish a diet-list that strictly conforms to the above principle, it will be found a most difficult problem to solve, owing to the very wide diffusion of starch and sugar throughout the organic world.

It has recently been claimed by Eickhorst, and others, that an exclusively nitrogenous diet is damaging to the organism in diabetes, and that the safer course is to permit a variety of foods, which includes the carbohydrates. Except in special cases, in which some organ is crippled by organic disease, such as the kidney, there is not a particle of evidence to support such assertion. It is well known that whole tribes of men live uninterruptedly upon an exclusive meat diet, and enjoy the most robust health, as well as a muscular and mental vigor that will compare favorably with those who live upon a mixed diet. Besides such examples upon a large scale, it has been demonstrated in private practice and experimental investigation, repeatedly, that a thoroughly nourishing and sustaining diet can be furnished, exclusive of the carbohydrates, upon which diabetic patients can live, not only without damage, but with uniformly beneficial results. In comparison with the damaging effects of sugar in the circulation, which is sure to result from the ingestion of starchy foods, the fancied damage due to the exclusive use of animal diet sinks into insignificance. We know that when the blood is charged with large quantities of sugar, it not only gravely alters the nutritive qualities of the former, but it is also liable to induce chemico-toxic changes in that fluid, which are dangerous to life. We know that the perverted elaboration of food (chiefly the carbohydrates), the saturation of the tissues with the resulting morbid products, and

the necessary efforts at their elimination, lead with certainty to altered nutrition, emaciation, wasting of the vital forces of the economy, secondary disease of important organs, and, in short, to that complex of morbid changes which in diabetes bring about exhaustion and death.

First in importance ranks the question of bread in the construction of any diabetic diet-list. The withdrawal of this article from the list is usually the most serious deprivation the patient has to encounter. In consequence of this fact, an almost endless number of breads have been placed upon the market, which are *claimed* to be free, or nearly free, from starch, and are hence named diabetic breads. Now, I do not hesitate to say that most breads which have been put upon the market with such claims are "a snare and a delusion," and have unquestionably shortened the lives of hundreds of diabetic patients. Most samples of so-called "diabetic flour," from which the starch is claimed to have been eliminated, "or nearly so," contain from 30 to 70 per cent. of that article. Some time ago I became very skeptical of these preparations, in consequence of finding, upon analysis of a sample coming from a prominent firm, that it contained about 60 per cent. of starch. But Dr. Chas. Harrington, of Boston, has rendered us under perpetual obligations to him for fearlessly exposing the most of these deceptions, by publishing a careful analysis of most of them in detail. It may first be noted that his analysis of home-made bread gives the proportion of contained starch as 44.99 per cent. The Graham wafer, made of Graham flour, contains 58.45 per cent. of starch. The gluten flour, of Farwell & Rhines, of Watertown, N. Y., contains 67.17 per cent. of starch. The special diabetic foods of these makers

contain 68.18 per cent. of starch; and the bread made of this flour would contain 36 per cent. thereof. The gluten flour of the New York Health Food Company contains 66.18 per cent. of starch. Bread made of this flour would contain 35 per cent. of starch. The gluten wafers of the same company contain 66.96 per cent. of starch. Dr. Johnson's "Educators," a biscuit said by the seller to be "absolutely free from starch," contain of the latter 71.42 per cent. The Boston Health Food Company's diabetic flour, No. 1, sold as absolutely non-starchy, contains 62.94 per cent. of starch. Bread made of this flour would contain 30 per cent. of starch.

In view of the above facts, there seems but one course to pursue with reference to bread if we expect to cure our diabetic patients, and that is to limit or curtail its use in all forms. By simply reducing the ordinary allowance of common bread to one-half the daily amount, we have it in our power still to furnish bread to the patient which gives him a less quantity of starch than does the use *ad libitum* of most diabetic foods in the market. After varied and laborious experiments with substitutes for bread, I have found the following method the most satisfactory: Permit the patient to use his own regular table-bread, but limit the allowance to one-half the usual daily use. If sugar still appear in his urine, reduce the allowance to one-quarter the ordinary amount. If sugar still appear in his urine, curtail the use of bread completely. The advantages of this method are that we know, with some degree of certainty, the amount of starch that the patient is getting in his bread-supply. The article supplied is, at least, digestible, which is more than can be said of most of the substitutes. In my experience, if the patient cannot assimilate one-half to one-quarter the usual amount of ordinary bread—

2 to 3 ounces daily—without excreting sugar in the urine, he cannot assimilate any substitute therefor, and, under such circumstances, the sooner all bread is stricken from his diet-list the better. When bread is permitted it should be as fresh as possible, and it is better cut in thin slices and well toasted on both sides. The daily allowance of bread will be better assimilated by diabetic patients if taken but twice a day,—at the morning and evening meals; the long intervals between its introduction into the stomach insure its more thorough disposal in the normal way.

Of the other foods derivable from the vegetable kingdom, the cereals and some of the tubers are the most dangerous. Potatoes, beets, parsnips, carrots, among the latter; and, of the former, rice, sago, oatmeal, cornmeal, buckwheat, rye, barley, peas, and beans, should be prohibited without compromise in most, if not in all, cases. In the strict form of dieting we are obliged to avoid the whole list. In cases of moderate severity we may, however, draw upon one class of vegetables—greens. Green vegetables consist mostly of cellulose, and contain little, sometimes almost no, starch. They are rendered still less objectionable if boiled before being eaten, as the hot water dissolves out much of the remaining starch and sugar. The starch and sugar contents of vegetables vary considerably, according to the degree of cultivation and the nature of the soil and climate in which they are grown. As a rule, a high degree of domestic cultivation favors an increase of the starch and sugar, while high temperature and sunny skies have an opposite tendency. Among the least objectionable vegetables may be mentioned lettuce, cucumbers, olives, mushrooms, brussells-sprouts, cabbage, spinach, and water-cresses.

Soja, or Japanese bean, owing to its high nutritive properties and its low percentage of starch, is likely to enter largely into the diabetic diet of the future. It has recently been much cultivated in some parts of Europe, especially in Hungary. Its composition is as follows: Nitrogen, 36.6 per cent.; fatty matter, 17 per cent.; starchy matter, 6.4 per cent.

A sauce is made from *soja* which bears the name of *stiso* and *soju*. A kind of cheese is made from it, and very much prized in Japan as a table-luxury.*

In Europe the soja has already been utilized for food of men and animals, and recently the attempt has been made to make bread of it. This is very difficult because of the large proportion of oil which it contains. This oil is very purgative, and hence it becomes necessary to rid the meal of it in order to render it fit for domestic usages. Lecerf in Paris and Bourdin in Rheims have succeeded in rendering the bread made from this meal very well supported by the stomach.

This bean, which, as the analysis shows, is more nutritive than meat, serves for nourishment to a great country like Japan, under the forms of sauce, of cheese, of farina, and even of *real* artificial milk.†

Most nuts except chestnuts may be permitted, the list including almonds, walnuts, Brazil nuts, filberts, butternuts, and cocoanuts.

Great differences prevail in practice with regard to the use of fruits in diabetic conditions, some authorities allowing them freely, while others curtail them. Some fruits, such as apples and strawberries, really contain very little sugar, and in the case of apples the sugar is

* See article of Egasse, on Economic and Therapeutic Applications of Soja, in Bulletin de Thérapeutique, vol. cxv, p. 133.

† Therapeutic Gazette, March 15, 1890, p. 150.

in such form that it is often well assimilated by diabetics. The truth is that it is more difficult to make a rule which will apply universally with regard to the use of fruits than with any other class of foods in these cases; and therefore it must to some extent be a matter of experiment in each individual case. It may be stated, however, in a general way, that mild cases will bear a moderate use of such fruits as apples, tomatoes, and strawberries; but in severe cases it is best to prohibit their use without exception.

With regard to foods of animal origin, fortunately but three articles are open to question as appropriate for use, viz., honey, liver, and milk. The first of these requires no comment further than to say that its highly-saccharine composition excludes it without exception from use in all cases. Liver contains a varying percentage of sugar, besides large quantities of glycogen, which is readily convertible into sugar, and therefore it is objectionable in strict dieting. Oysters must be included in this restriction, owing to their proportionately enormous livers.

With regard to the propriety of the use of milk, authorities differ very greatly. Dr. Donkin, the most enthusiastic advocate in its favor, published a book in London, in 1871, upon the exclusive use of skim-milk as a cure for both diabetes and Bright's disease, and since then the "milk cure" has attracted considerable attention. Dr. Donkin's method of treating diabetes by a milk diet, however, has met with but feeble indorsement by his own countrymen, most of whom either limit or exclude it from use. On the other hand, Dr. Tyson, of Philadelphia, whose experience has been very large in these cases, very strongly indorses the milk cure. My own experience with the use of milk in the treatment of

diabetes began nine years ago, since which time I have made thorough and varied trials of it. My conclusions are that a milk diet is successful, chiefly, in milder forms of the disease. Such cases are, as a rule, controlable by moderate limitations of diet, which offer a greater range and nutritive power than does milk. I believe that the milk treatment, therefore, finds its most appropriate range of application in cases of children, and those cases which are complicated by renal lesions—albuminuria.

I have searched in vain, among the published cases which Dr. Donkin has treated by skim-milk diet, for a single record of cure; nor have I found any result that could be called at all remarkable, as compared with those treated by an animal diet. Dr. Donkin's "Case I, J. G., complete recovery," so called, must be considered the best result obtained. This was a case in which, upon skim-milk diet, the urine became free from sugar, and so remained thirteen months; but here the record ends without the patient ever having returned to a mixed diet, save the addition of meat. Now, when we consider that J. G. was "a large, robust man, 58 years of age," we would at once expect that a very moderate restriction of carbohydrate foods would eliminate the sugar from his urine. Certainly, as a rule, we can readily eliminate the sugar from the urine, in cases of that age and type, by very moderate restrictions of diet. Dr. Donkin's young diabetic patients, according to his own records, without exception, ultimately died from some typical complication of the disease, as pneumonia, phthisis, or bronchitis,—as did his cases III, IV, and VI; and moreover, as a rule, they continued to excrete more or less sugar with their urine, although he speaks of these cases as examples of "rapid and complete recovery," "immediate relief and arrest of the disease," etc.

The facts appear to be, with regard to milk, that it acts by reducing—not curtailing—the sugar-convertible food. Milk contains about ½ ounce to each pint of lactine (milk-sugar), an animal hydrocarbon, which I do not doubt, as Dr. Pavy says, "comports itself in the intestinal canal precisely as does grape-sugar." It has been claimed that lactine is changed in the stomach into lactic acid, and thus escapes sugar transformation; but the fallacy of this doctrine may be readily proved by administering lactine to patients affected with pronounced diabetes, when without exception it will be found to quickly increase the excretion of sugar by the kidneys. The oft-repeated statement that milk-sugar is well assimilated by diabetics, in my experience, only holds true in mild cases. In the more severe type of the disease an exclusive or even adjunct diet of milk has invariably been attended by unsatisfactory results.

In the matter of beverages, I am satisfied that diabetic patients are usually permitted greater liberties than is good for them; indeed, I do not doubt that the excessive use of the highly-saccharine wines often has much to do in bringing on the disease.

Until very recently, when I took the pains to analyze most of the beverages in domestic use, I was in the habit of permitting the usual stereotyped list. I find, however, that many of them which are usually allowed contain very considerable amounts of sugar, and I now exclude them from use, with perceptively good results to my patients. Thus, coffee is permitted in all the diabetic diet-lists I have seen, and yet the best grades of Java and Mocha contain at least 10 per cent. of sugar. By taking ½ ounce of Java coffee commonly sold in the markets, and with a cup of boiling water I have made the usual cup of coffee in domestic use. Analysis

of this cup of coffee demonstrated that it contained 1.5 per cent. of sugar—about 7½ grains to the fluidounce. Analysis of Mocha gave closely corresponding results.

With regard to alcoholic beverages, it is doubtful if their temperate use is harmful to diabetic patients, provided they be free from sugar. The importance, however, of the last-named point cannot be too strongly insisted upon, and, since I have carefully analyzed most of the list, the following results are subjoined as a guide in practice:—

SUGAR CONTENTS OF LEADING ALCOHOLIC BEVERAGES, ACCORDING TO THE AUTHOR'S ANALYSIS.

	CONTENTS OF SUGAR IN EACH FL. OUNCE.
NATIVE AMERICAN WINES.	
H. W. Crabb's California.	
Chablis,	1 grain.
Rislings,	1 "
Sauterne,	1.3 grains.
Old Grape-Brandy,	4 "
Burgundy,	3–4 "
Cabernet, Medoc, Beclan, } Clarets,	2–3 "
Sherry, Old Dry,	10 "
Marsala,	10 "
Madeira,	24 "
Port, Old,	34 "
Tokay,	48 "
Muscatel,	80 "
Malaga,	40 "
Angelica,	50 "
Steuben County Wine Co.'s Wines.	
New York Catawba,	1 grain.
Ohio Catawba,	1 "
Ohio Delaware,	3 grains.
Norton's Virginia Seedlings,	4–5 "
Burgundy,	5–6 "
Extra Family Claret,	3–4 "
Walters' Sherry, Dry,	8 "
P. J. Port, Dry,	24 "
Gold Cross Champagne,	30 "

IMPORTED WINES.	CONTENTS OF SUGAR IN EACH FL. OUNCE.
Port, Oporto,	30 grains.
Sherry, Vino de Pasto,	12 "
Malaga,	140 "
Madeira,	45 "
St. Julien,	2–3 "
Pontet Canet,	4–5 "
Chateau Larose,	4–5 "
Budai Imperial* (L. Reich, N. Y.),	None.
Diatetischer Rothwein* (Schreiber's),	"
Rhine and Moselle Wines.	
Deinheimer,	1 grain.
Niersteiner,	1 "
Geisenheimer,	1 "
Cardens,	1 "
Laubenheimer,	1 "
Liebfraumilch,	1 "
Marcobruner,	1 "
Johannisberger,	1.5 grains.
Sauternes.	
Graves,	12 grains.
Haut Sauternes,	10 "
Sauternes,	20 "
Barsac,	17 "
Burgundy Wines.	
Beaujolais,	4–5 grains.
Chambertin,	4–5 "
Pommard,	5–5.5 "
Champagnes.	
Pomery Sec,	30 grains.
G. H. Mum's Extra Dry,	30 "
Veuve Clicquot,	30 "
Ruinart, Extra Dry,	12 "
Ruinart, Brût,	10 "
Moët & Chandon's Imperial Brût,	15 "
Piper Heidsieck, Sec,	30 "
Roederer, Carte Blanche,	48 "
Monopole Club, Dry,	20 "

* The Budai Imperial of L. Reich, New York, and the Diatetischer Rothwein of Loeb & Co., 55 Warren Street, N. Y., are the only wines I have found absolutely free from sugar in the market.

	CONTENTS OF SUGAR IN EACH FL. OUNCE.
Drp Monopole,	30 grains.
Delbeck, Extra Dry,	8 "
Delbeck, Brût,	10 "
Perier Joučt, Special,	34 "
Jules Mum's Grand Sec,	40 "

SPIRITS.

Jamaica Rum,	7.5 grains.
St. Croix Rum,	None.
Medford Rum,	"
Gin, Old Tom,	"
Gin, Holland,	"
Brandy, Hennessy,	2.5 grains.
Brandy, Reno,	4 "
Whisky, Scotch,	None.
Whisky, Bourbon,	"
Whisky, Rye,	"
Whisky, Irish,	"
Arrack,	"
Tequila (Mexican),	24 grains.

BEERS, ALES, AND PORTERS.

Domestic Beers.

Schlitz's Pilsener,	4 grains.
Schlitz's Extra Pale,	4 "
Schlitz's Export,	4 "
Schlitz's Porter,	7.5 "
Blatz's Export Beer,	4 "
Pabst Beer,	5 "
Schoenhofen Beer,	4.6 "
U. S. Brewing Co.'s Beer,	5 "

Imported Beers.

Pilsener, Light,	3 grains.
Erlanger, Dark,	6 "
Liebotschaner (Bohemian beer),	2 "
Capuziner,	4 "
Augustiner,	6 "
Wurzburger,	5 "
Culmbacher,	6 "
Tivoli,	5 "
Budweiser,	5.8 "
Kaiser,	2 "

	CONTENTS OF SUGAR IN EACH FL. OUNCE.
Ales.	
Bass,	2 grains.
Allsop's,	2.5 "
Dow's,	3 "
Porter.	
Guinness's stout,	6 grains.

It will be seen, from an examination of the foregoing list of alcoholics, that, of the wines, the Rhine and Moselle type is the most suitable for the use of diabetic patients on account of the very low percentage of sugar which they contain,—only 1 to 1.5 grains to the fluid-ounce. Special attention is called to the fact that a number of native American wines of this type—notably Chablis and Rislings of California, and the catawbas of New York and Ohio—are nowise inferior in this respect to the very best brands of imported wines; indeed, they are considerably superior to some of the most expensive Rhine wines, such, for instance, as Johannisberger. For the plethoric diabetic patient, therefore, the American wines just named may be considered very suitable. On the other hand, in the spare and anæmic class of patients a red wine is more suitable, and in this class no wines approach the Budai Imperial and Diatetischer Rothwein, since they are probably the only clarets in our market that are free from sugar.

Of the various spirits, rum should be avoided, as probably most brands contain more or less cane-sugar, and in the case of Jamaica rum a very considerable percentage of grape-sugar is also present. Brandy contains a varying amount of sugar, as usually found in the markets, ordinarily from 2 to 5 grains to the ounce. It should therefore be used but sparingly. Whiskies are free from sugar.

With regard to beer, ale, etc., the grape-sugar added

in manufacture for fermentative purposes is never thoroughly removed by the latter process. Bass's pale ale and the pale Bavarian beers contain the least amount of sugar of this class—about 2 grains to the ounce. The quantity of these beverages usually drunk quite makes up for the quality, and therefore, on the whole, they are best used but sparingly by diabetic patients, or altogether avoided.

Champagnes, sauternes, and sweet wines—either native or imported—are altogether unsuitable for the use of diabetic patients, as will be readily seen upon examination of the list.

All mineral waters are permissible as beverages, and some of them are curative, especially the alkaline waters.

Among the American waters, those of Waukesha, and especially the Bethesda Spring, stand at the head of the list. The best results are derived from these waters by drinking them at the springs for a few weeks, where I have invariably found them to be beneficial to diabetic patients. The Saratoga Vichy is also an excellent water; its alkalinity renders it especially suitable in these cases. Finally, the Idaho Springs, near Denver, especially the Bath Spring, deserves mention as approaching closely in composition the Carlsbad waters in Bohemia, though of somewhat lower temperature.* With such excellent and appropriate waters at home, it seems not only foolish but hazardous that so many of our countrymen should undertake the risks, inconveniences, and expense of long pilgrimages to European springs, for it is well known that such long, fatiguing journeys are peculiarly dangerous to diabetic patients.

Having, in a general way, reviewed the leading

* Unfortunately, the high altitude of the Idaho Springs renders that location unsuitable for lengthy visits by diabetic patients.

features of the dietetics of the disease, a list of appropriate foods is here appended as a more minute guide, followed by a list of those which should be prohibited.

Foods Permitted.—Meats of all kinds except livers,—beef, mutton, pork, poultry, game; either fresh, roasted, broiled, dried, smoked, cured, potted, or prepared in any way except with sugar, flour, or prohibited vegetables. Soups made from meats without flour and excluded vegetables. Fish of all kinds except oysters and the inner parts of crabs and lobsters. Eggs, butter, cheese, and oils. Jellies made from Cox's gelatin, unsweetened except with saccharin. Spinach, lettuce, olives, cucumbers, summer cabbage, mushrooms, brussells-sprouts, and water-cress. Almonds, filberts, walnuts, cocoanuts, and Brazil nuts.

Beverages.—Water, including all mineral waters, Rhine wine, California Rislings and Chablis, New York and Ohio catawbas, Budai Imperial, Schreiber's "dietetic wine," whisky, and gin.

Foods Prohibited.—Common bread, except as specified below; biscuits, crackers, and cakes. Farinaceous articles, such as potatoes, rice, sago, tapioca, macaroni, vermacelli, common flour, oatmeal, cornmeal, buckwheat-flour, barley-meal. The liver of all animals, oysters, and sugar. Saccharine vegetables, as turnips, carrots, parsnips, peas, beans, beets, onions, and rhubarb. Blanched vegetables, as celery, seakale, endive, radishes, and all roots, fruits, and chestnuts.

Beverages.—Tea, coffee, milk, whey, buttermilk, skimmed milk, chocolate, cocoa, malt liquors, cider, champagne, sauternes, sherry, port wine, Madeira, and all sweet wines and liquors.

The discovery of saccharin has furnished us a substitute for sugar which has a sweetening power of nearly

three hundred times greater than the latter. The tablet form in which saccharin is now put up is very convenient for sweetening beverages. My patients have usually found that food and beverages flavored with saccharin, if not oversweetened, are quite as agreeable and pleasant as when flavored with sugar.

Systematic Method of Dieting.—A systematic method of dieting diabetic patients is of no less importance than the quality of the diet employed. In order to determine accurately the effects of certain foods upon the disease, no specific medication should be employed until the sugar excretion is reduced as far as possible by diet alone. This method enables the physician to distinguish how far improvement is due to diet and how far to the medication, the practical importance of which will be readily perceived.

When a case first comes under observation, it is a useful plan to permit the patient to eat and drink whatever he chooses for the first twenty-four or forty-eight hours, in order to gauge the character of the disease. At the end of that time careful note should be taken of the quantity and specific gravity of the urine, as well as the percentage of sugar. In beginning treatment, an abrupt change to a strict diabetic diet would carry with it more or less danger, and therefore such course is not advisable, but rather a gradual change should be brought about. Step by step the more objectionable foods should be limited or cut off until sugar ceases to appear in the urine, or until we reach an exclusively animal diet.

The first step should consist in excluding the use of potatoes, sugar, and farinaceous foods, and reducing the bread-allowance to one-half the usual amount eaten by the patient—$3\frac{1}{2}$ to 4 ounces daily. With these restrictions the patient may continue without other changes for about

two weeks. In the milder cases this "first step" in dieting will have caused a reduction of the sugar in the urine to relatively small proportions; indeed, in many cases it will disappear. If, however, at the end of two weeks sugar still appear in the urine under close observance of the above restrictions, we may know that the disease is at least of fairly severe type, and we should proceed to the next step in dieting. This should consist in the exclusion of milk and all vegetables except the green ones enumerated in the permissible list. Greater care should be exercised in the use of bread; not more than one small slice should be permitted at the morning and evening meals,—2 ounces daily. Perhaps one apple a day, if not sweet, may be allowed; one tomato, or, in place of the latter, a few strawberries. The urine should be examined from time to time, and if sugar does not disappear the restrictions should be increased until the patient is living upon meats, a few greens, and some nuts, and but 1 ounce of bread daily, with water and the permissible alcoholics as beverages.*

After three or four weeks' adherence to the above restrictions, if sugar still appear in the urine, we may be sure that we have to deal with the disease in its most severe type, and, accordingly, we must bring to bear against it all our resources of diet in the strictest form. Everything containing starch or sugar that can be avoided should be strictly prohibited; in short, the patient should be reduced to an absolute animal diet. Meats, gelatin, eggs, and fish should constitute exclusively the food, while water and a little spirits should be the limit of beverages.

It will be found that a strictly animal diet will often

* It will be found that a slice of freshly-made table-bread ¾ inch thick and 3 inches in diameter, if nearly circular, will weigh about 1 ounce.

remove the last traces of sugar from the urine; and after continuing it for a few weeks or months, a reversion to some of the less objectionable articles of the vegetable order will cause no re-appearance of sugar in the urine.

It must not be supposed that it is always an easy matter to place patients upon an absolute animal diet. Aside from the difficulties of securing the thorough accord and assistance of the patient, those especially with weak digestive powers frequently suffer from gastric disturbances and diarrhœa. When such complications arise the diet must be relaxed a little, and the patient should be brought more gradually under restrictions. Time and patience will, in the majority of cases, overcome all obstacles. I once labored with a young diabetic patient for about four months in accustoming his stomach to an animal diet, upon which he now lives in perfect contentment and excellent health, with his urine free from sugar, now considerably over a year.

In accustoming patients to a diabetic diet, care should be exercised not to permit the stomach to be overloaded with food, light meals being the better rule to follow. The beneficial effects of temperate eating in diabetes were prominently illustrated during the siege of Paris, as Bouchard tells us that sugar entirely disappeared from the urine of diabetics in whom up to that time it had persisted, even though they had been living on a carefully-regulated diet. The diminution in the quantity of food, occasioned by its great scarcity during the siege, effected that which alteration in quality had failed to accomplish.

In stout, overnourished diabetics of middle age and over, the disease often yields completely to habits of moderate or spare eating. The disease in such cases is doubtless brought about by overeating, for, as a rule,

such patients are large eaters. If in these cases the amount of food be reduced to a limit which the system can appropriate, without even altering the quality thereof, the disease will pass away; and, moreover, if habits of temperance in eating and drinking be continued, the cure will usually be permanent.

About two years ago a patient withdrew from my care because I did not give him medicine to remove the sugar from his urine. The percentage of sugar in his urine was small, and was due to intemperate habits of eating and drinking, which he could not be induced to correct. It was no uncommon occurrence for him to eat all the luxuries and delicacies within the range of a well-appointed table, and to imbibe therewith a quart or two of champagne, and finally to finish the day with a plebeian potation of eight or ten glasses of lager beer. He has since made one or two trips to Carlsbad, but without essentially altering his habits, and it is needless to add that he still has his diabetes. Like too many wealthy men, he evidently lives up to the belief that his money should procure him not only all the luxuries of life, but also exemption from the ills of "the world, the flesh, and the devil."

With regard to the use of water by diabetics, I have usually placed no limit upon the quantity allowed, permitting the patient to follow his own inclinations in this respect, only stipulating that it should not be drunk ice cold. The increased thirst of diabetics points to dehydration of the blood and tissues, and it is more than probable that the liberal use of water serves a useful purpose in taking up and carrying sugar from the system, which might otherwise accumulate sufficiently to give rise to serious consequences.

The dietetic treatment of diabetes has been dwelt

upon at considerable length because, with our present knowledge, it undoubtedly holds the key to the most successful management of the disease. In concluding this review of dietetics, the importance of at first separating this from the medicinal treatment cannot again be too strongly insisted upon, since, as already shown, when a system of diet and medication are employed simultaneously from the beginning, it is impossible to estimate, with any degree of accuracy, the beneficial effects of either the one or the other. When we have accomplished all that seems possible with the aid of diet, if sugar still remain in the urine, *then*, and *only then*, should we have recourse to drugs, unless it be to combat special symptoms.

Medicinal Treatment.—It remains next to speak of the medicinal treatment of diabetes, and, of the extended list of drugs which have been from time to time extolled for their curative powers over the disease, only those will be considered which have met with sufficient indorsement to entitle them to notice.

Opium.—Considering the decided nervous element in the causation of diabetes, it would naturally be expected that nervous sedatives would have some controlling influence over the disease. To some extent these anticipations have been realized, since opium, as the representative of this class of drugs, tends to restrain the excretion of sugar; indeed, of the various drugs that have been recommended, opium maintains its reputation best. To be effective, opium must be employed in full doses, and therefore it is fortunate that diabetic patients, as a rule, are remarkably tolerant of the drug.

The indications for the employment of opium are a continued high percentage of sugar in the urine, which

fails to yield to strict dietetic measures. In such cases it may be administered in gradually increasing doses until the sugar disappears from the urine, or until no further reduction in the percentage of sugar seems to be obtainable. As to the method of administration, I believe Dr. Ralfe's practice, of giving one sufficient daily dose at bed-time, to be the most useful. This is least likely to disturb the digestion, or to cause the patient headache and other disturbances. Of the various preparations of opium, *codeine* is probably the most useful, as it is less likely to induce constipation than the crude drug, and, moreover, it is much better borne by the stomach. The dose, to begin with, should be $\frac{1}{4}$ to $\frac{1}{2}$ grain, which may be gradually increased to from 5 to 15 grains per day. Morphine, or, better still, the bimeconate of morphine, may be employed if codeine be not obtainable.

It must not be forgotten, however, that in opium we have an agent capable of doing much harm if recklessly employed. Its prolonged use is liable to induce the opium habit, and, although the danger of the latter is said to be diminished in diabetics, it is still a danger which no condition confers complete immunity from; and this applies both to opium and its preparations. The dose required to control the excretion of sugar is usually so large that, sooner or later, in my experience, the drug has to be abandoned on account of its damaging effects upon nutrition. The exceptions to this rule, I am satisfied, are so few that the opium treatment should be reserved, for the most part, for failures by other methods.

Antipyrin.—Somewhat allied to opium may be classed the recently introduced agents of the phenol and aromatic series,—antipyrin, phenacetin, salol, acetanilid, exalgin,

etc. Antipyrin, the most powerful and most popular of these, has been heralded as almost a specific for diabetes. Like so many alleged specifics for diabetes in the past, it is likely to enjoy a season of popularity and then pass into merited oblivion. The first case that I treated with antipyrin was one of typical severity, in a young subject in whom careful dieting had kept the urine down to an average of 4 pints daily, and a varying percentage of sugar of from 2 to 5 grains to the ounce for many months. All restrictions of diet were thrown off, and the patient was put upon 45 grains of antipyrin a day. The quantity of urine and the percentage of sugar steadily increased from the beginning. At the end of ten days the sugar had reached about 15 grains to the ounce, and three days later the patient passed into typical diabetic coma and rapidly succumbed.

The second case was quite as typical, although in an older subject. The sugar had been reduced to 1 per cent. or under by careful dieting for two years. Dietetic restrictions were only partly relaxed, and under 45 grains of antipyrin a day the quantity of sugar doubled, as did also the volume of urine, by the end of one week. The third case was one of glycosuria, in which, upon a strict diet, the urine was usually free from sugar. Upon relaxation of diet rules, sugar appeared in the urine to the extent of 2 or 3 grains to the ounce, which antipyrin failed to eliminate at the end of a week.

Antipyrin is unsuitable for lengthy periods of administration in doses of 45 grains per day, and in smaller doses it is not claimed to modify the disease. Moreover, it is liable to cause albuminuria, and therefore it cannot be considered a safe agent for use in these cases.

The *bromides* have long been used in the treatment of diabetes. They are excellent remedies for many ner-

vous conditions which so often accompany the disease; but I have never been able to trace any reduction of sugar in the urine to their use. It is possible, however, that they may indirectly contribute toward a lessened degree of sugar excretion by inducing a more tranquil nervous state. The bromides of sodium and lithium are preferable to the potassium salt, being more acceptable to the stomach. The bromide of sodium is given in 15- to 20-grain doses, and the lithium salt in 5-grain doses, well diluted, and the dose may be repeated several times a day.

Ergot has enjoyed a popularity in the treatment of diabetes second only to that of opium, and probably not without some slight merit. Its vaso-constrictor action upon the portal circulation doubtless accounts for its beneficial effects in these cases. Its controlling power over typical diabetes, however, is feeble; but in mild cases it often sensibly diminishes the sugar excretion. Ergot is, therefore, best suited to mild cases, and especially those in which the patient has good digestive powers. The drug is best administered in the form of ergotine, or the fluid extract of ergot prepared by Squibb. The latter may be given in $\frac{1}{2}$-drachm doses, gradually increased according to the tolerance of the stomach.

Arsenic has long been used in the treatment of diabetes. Its use was first suggested from the fact noted by Salkowsky, that when animals were given large doses of arsenic, glycogen greatly diminished in their livers. More recently bromide of arsenic has been strongly recommended in doses of $\frac{1}{40}$ grain, which may be increased to $\frac{1}{20}$ grain, or more, if no toxic symptoms are observed. There are two standard solutions of bromide of arsenic in the market,—Giliford's,

of which the dose is 10 drops to begin with, which may be increased to 20 drops, or over; and Clemen's solution, which is considerably stronger, and the dose of the latter, to begin with, should not be over 5 drops. A few years ago it was thought that bromide of arsenic promised brilliant results in diabetes, but it must be confessed that it has disappointed expectations. In one of my cases Giliford's solution was given for a long time, in 25-drop doses three times a day, but during all this time the patient continued to excrete urine that contained 30 grains of sugar to the ounce. Upon withdrawing the bromide of arsenic, and placing the patient upon a restricted diet, I had the satisfaction of seeing the sugar speedily reduced to 2 or 3 grains to the ounce. I have given the bromide of arsenic treatment a thorough trial, in at least 10 or 12 other cases, without obtaining any result which could be called satisfactory; certainly, it has not materially lowered the percentage of sugar in the urine. In conjunction with lithium, as suggested by Rouget, arsenic has attained some popularity, being especially lauded by Martineau, who claims to have cured 67 out of 70 cases of diabetes by this treatment. In other hands, however, this treatment has not been attended by appreciable benefit; at least, such is the report from Bordeaux, where opportunities for trying it on a large scale have been carried out. The chief benefits I have obtained from the use of arsenical preparations in diabetes have been from arsenite of iron, in cases complicated by anæmia or malaria. In such cases I often employ the latter, in pill form, beginning with $\frac{1}{16}$ grain, and gradually increasing the dose to $\frac{1}{8}$ or $\frac{1}{6}$ grain.

Iodoform was recommended by Moleschott, about ten years since, as a remedy for diabetes. Since then

it has been used considerably, and with somewhat favorable results, seeming to cause a diminution of thirst, polyuria, and the excretion of sugar in the urine. Its well-known tendency to produce toxic symptoms renders great care necessary in its administration. Its use should, therefore, not be continued beyond two weeks at a time; but after two weeks' interruption it may again be resumed for another two weeks. Iodoform may be given in doses of 1 to 3 grains, repeated three times a day; or one sufficient dose may be administered at bed-time, which is probably the least unpleasant method. Moleschott's formula, which is claimed to disguise the unpleasant odor of the drug, is as follows: Iodoform, gr. xv; ext. lactucari sat., gr. xv; cumarin, gr. iss; to be made into 20 pills.

Jambul.—The seeds of the *Syzygium jambolanum* are highly extolled by the natives of India as a remedy for diabetes. The jambul treatment was introduced into Europe about five years ago, and has met with varying success. The drug appears to be very uncertain in its action as obtained here, occasionally giving very good results, or apparently so, while at other times it seems to exert no favorable influence over the disease. I have certainly observed marked benefit from it in one chronic case, as it completely eliminated the sugar from the urine, while the patient was on a non-restricted diet. I have since used it in a number of other cases, but with much less satisfactory results. The dose of the powdered seeds is from 3 to 5 grains. A fluid extract of jambul is prepared, the dose of which is from 6 to 8 drops.

Oxygen.—Inhalations of oxygen gas have been strongly recommended for diabetes by Bouchard, Day, Demarquay, Wallian, and others. My own experience

with this agent has led me to think very favorably of its use in these cases. I have already shown that diabetes is a much less fatal disease in low altitudes, and, moreover, the evidence may be considered conclusive that the increased oxidizing power of the blood consequent to low altitudes is the chief cause of this favorable influence over diabetes. By the systematic employment of oxygen inhalations we may secure the same beneficial results to our patients at home which are afforded by a residence at or near the sea-level. In my hands, the best results in these cases have followed upon the inha-

lation of from 3 to 5 gallons of oxygen twice daily,—morning and afternoon. The gas may be more economically, as well as more effectually, administered by diluting it with about an equal volume of atmospheric air, and inhaled slowly and deeply, half a minute or so elapsing between the inhalations.

Various appliances have been devised for the generation and administration of oxygen, but for the use of those in general practice the apparatus furnished by the American Oxygen Association of New York, under the name of No. 1 (see cut, above), is, altogether, the best

in the market. This apparatus has a capacity of 8 to 10 gallons in ten minutes,—sufficient for 2 doses,—and the oxygen furnished is remarkably pure. The instrument is as portable as an ordinary hand electric battery, and may, therefore, be used in the office or at the home of the patient.

Another, though far less efficient, means of obtaining the benefits of oxygen is by the administration of dioxide of hydrogen, or so-called peroxide of hydrogen. The dioxide of hydrogen is usually administered in the form of a 3-per-cent. solution,—preferably Marchand's,—the dose of which is from 1 to 2 teaspoonfuls, largely diluted with water. A better article still is the glycozone of the same manufacturer. Those who desire to make themselves more thoroughly acquainted with recent methods in the use of oxygen are referred to the excellent work of Demarquay, on "Medical Pneumatology," recently translated, with valuable additions, by Dr. Wallian.

Alkalies.—Finally, the beneficial effects of the administration of alkalies in diabetes deserves mention here. The blood in diabetes becomes greatly reduced in its alkalinity, and, as a consequence, its oxygen-holding powers are greatly weakened. It follows, therefore, that the use of alkalies are very appropriate in these conditions, and experience has amply demonstrated their usefulness.

A number of other drugs have been more or less highly extolled for their alleged specific influence over diabetes. Among these may be mentioned: *Sodium phosphate, nitrate of uranium, salicylic acid, picric acid, calabar-bean, potassium iodide, iodine tincture, lactic acid, codliver-oil, belladonna, valerian, and phosphorus.* There does not appear to be sufficient evidence in favor

of any of these to entitle them to any degree of confidence. Carefully discriminated from the benefits derived from dieting, these drugs are probably nearly inert, so far as their influence over diabetes is concerned.

Treatment of Complications and Special Symptoms.—It remains next to consider the treatment of the special symptoms and complications of the disease. Those referable to the stomach command special attention, since disordered digestion is so frequent an accompaniment of diabetes that it may be considered the rule, after the disease has become thoroughly established. The digestive and assimilative functions should, therefore, receive special support, through such agents as general experience has taught us prove the most efficient. Among these may be mentioned pepsin, the vegetable bitters,—especially strychnia,—and the mineral acids.

Constipation of the bowels, so frequently accompanying the disease, should be especially guarded against, as this condition reacts very markedly, in enfeebling the digestive and assimilative powers. In addition to this, it is believed that constipation often tends to precipitate diabetic coma. I have an especial preference for the natural alkaline purgative waters to meet the requirements in such conditions, since they relieve the overacid state of the intestinal canal, so common to the disease. Freidrichshall water; or the recently-introduced Spanish Rubinat Condal water, given before breakfast, are very appropriate; or 1 or 2 teaspoonfuls of Sprudel salt may be taken in a glass of hot water, upon rising in the morning. In middle-aged people inclined to stoutness and overeating, a course of purgation by either of the above-named agents often proves highly beneficial.

An occasional purgative dose of blue mass (10 grains)

has an admirable effect at times. The continued action of small doses of mercurials is justly open to question in these cases; but when an occasional decided dose is given, the liver is stimulated to clear away the effete bile products, and the assimilative powers of the intestinal tract are improved by the relief afforded to the sluggish portal circulation.

The pneumonic and inflammatory bronchial complications are best met by such agents as ergot, combined with digitalis and muriate of ammonia.

Furuncles.—The complication of multiple boils sometimes yields to quinine, when given to the extent of 10 or 12 grains daily. They are sometimes very chronic and rebellious to treatment, however, in which case the only certain relief to be obtained is by eliminating the sugar from the urine, and every effort should be made in that direction.

Diabetic Coma.—The most dangerous, and certainly the most rapidly fatal, of all the complications of diabetes is that of Kussmaul's coma—sometimes, though I think improperly, called acetonæmia.

Dr. Ralfe, who has studied this subject closely, advises, in the early stage, a vapor bath given in bed, and the use of powerful stimulants, as ether, ammonia, musk, valerian, and camphor. He records a case in which he rescued a patient from a threatened attack by the prompt administration of a hot bath. Temporary improvement has followed the intra-venous injection of sodium-carbonate solution in these cases. Thus, J. Hesse has recently injected a 4-per-cent. solution of sodium carbonate into the veins of a comatose diabetic, with the result of a decided improvement for some hours. The patient relapsed into coma, however, but was again relieved by injection of 8 ounces more of the

sodium solution. The patient, after twenty-four hours, had a third attack, from which he died. Dickinson has recently recorded a very similar case.

If the conclusions which I have reached as to the causation of diabetic coma be correct, viz., as elsewhere stated, that the condition is due to the toxic influence of ptomaines, then the inhalation of oxygen gas would seem to offer the best chances of relief in such cases. I regret that, since I began the use of oxygen in the treatment of diabetes, I have not had opportunities for observing the effects of oxygen inhalations over diabetic coma, for they seem to me altogether likely to be capable of affording substantial relief in such cases. I do not regard the temporary benefits derived from intra-venous injections of alkalies in diabetic coma as due to their neutralizing effects upon acetone in the blood, but rather to their increasing the oxidizing powers of that fluid, which alkalies are well known to do. In diabetic coma, therefore, I should employ the sodium-carbonate injections, as has been the practice heretofore, but I should also re-inforce these by the most liberal inhalations of pure oxygen gas.

Since the treatment of diabetic coma has thus far proved so unsatisfactory, the physician should be constantly on the alert for its early indications, in order that every possible means may be employed to prevent its appearance. In advanced cases, especially if emaciation be marked and progressive, the patient may be considered in constant danger. Constipation, mental emotion, and fatigue should be avoided. Any unusual illness, however slight, but especially in the way of gastric disturbance, should be the signal for confinement in bed, and appropriate treatment to prevent the attack.

In conclusion, it seems desirable to emphasize the immense importance of careful dieting, as greatly outweighing all our other resources against the disease combined. This fact should be strongly impressed upon the patient from the beginning. He should be taught to rely but little upon medication, and the most effectual means of accomplishing this is to teach him how much can be achieved by careful dieting alone. When he has once learned through experience that the amount of sugar in his urine always bears a direct ratio to the quantity of prohibited foods indulged in, he is less likely to overstep the proper limits imposed. Diabetic patients are proverbially intelligent people, and with their thirst, polyuria, and other discomforts relieved, a sure sequence in most cases of careful conformance to the diet rules, unless greatly lacking in gratitude they will cheerfully submit to the restrictions imposed.

Hygienic Treatment.—In the hygienic management of diabetes two points should be constantly kept in view: the lowered bodily temperature, and the reduced oxidizing powers of the economy. In order to compensate for the first, these patients should be clad in pure-wool under-garments (all wool) from head to foot, thus economizing the body-heat as far as possible. To meet the second indication, the respiratory apparatus should have the widest possible scope, thus to facilitate as perfect oxidation by the lungs as possible. The patient should live as much as practicable in the open air, and on no account should he live or sleep in small rooms or confined atmosphere. His chambers should be thoroughly ventilated by night as well as by day, without, however, being permitted to become cold. Both the indications above-named are more easily attained by a residence in warm climates, near the sea-level, the par-

ticular location of which will be seen by referring to Section I, where this subject has been systematically considered.

Warm-water baths are very beneficial to these patients, and they may be rendered more efficient by the addition of some alkali, such as sodium bicarbonate. These baths should be repeated frequently, and they may be followed by thorough rubbing of the skin by means of brushes or coarse towels. On no account should cold plunges or sea-baths be indulged in.

A moderate degree of exercise in the open air is usually beneficial; at the same time, care should be taken to prevent great fatigue. The dangers of overexertion are well known, and especially in elderly and debilitated subjects it is unwise to permit overexercise. The cares and anxieties of business, especially if exacting, should, if practicable, be exchanged for more moderate and cheerful employments, or, better still, thrown aside, and a period of rest and relaxation indulged in.

Habits of regularity in eating, drinking, and sleeping should be established. The question of sleep is of special importance, for, as a rule, diabetic patients do not sleep well. At least seven or eight hours' sleep should be secured each night, as the tranquilizing influence of sleep upon the central nervous system secures a more stable control of nerve-force in the vasomotor tract. The noise and distractions of city life are unsuitable because of the constant tension and waste of nervous force. These should be substituted, when practicable, by the quiet of country life, more especially in the summer months.

SECTION VII.

CLINICAL CONSIDERATIONS.

In order to better illustrate the clinical features of saccharine diabetes, as well as to demonstrate the influence of treatment over the disease, the following cases are subjoined from my records of private practice.

Cases of Severe Type in Young Subjects.—The first 3 cases may be taken as fair average types of the disease as usually found in young subjects, showing the features of severity and intractability to treatment almost universally characteristic of the disease in such patients.

Case 108, J. L.—*December 10, 1885.* Patient's age, 29 years. He states that his general health has always been good; that he never had any serious illness. He has been very actively employed in business since he was 18 years old. He first noticed weakness and debility in September last. He has suffered from dyspepsia, more or less, for a year. He has been rising at night to urinate for the past three weeks, and he has noted very pronounced thirst of late. Examination of his urine shows a specific gravity of 1045, reaction sharply acid; sugar is present in quantity between 5 and 6 per cent. The urine is free from albumin. He was ordered nitro-muriatic acid, dil., 10 drops, with strychnia, $\frac{1}{40}$ grain, three times daily, for his dyspepsia; the diet to be gradually restricted to meats, green vegetables, and a small amount of bread.

December 18th. The quantity of urine is much reduced; its specific gravity is 1030, and the quantity of sugar present is about 2 per cent. He no longer rises at night to urinate, and his thirst has subsided.

January 11, 1886. The patient passes, by measure, 118 to 134 ounces of urine daily. The specific-gravity range is 1035; sugar, about 2 per cent.

February 5th. His condition seems somewhat improved. The quantity of his urine averages 80 ounces daily; the specific gravity, 1033, sharply acid in reaction, and it contains no albumin, but sugar is present in quantity of 6 grains to the ounce. His diet is restricted to meats, green vegetables, fish, eggs, gelatin, and one small slice of bread a day. He was now put upon arsenite of iron, $\frac{1}{16}$ grain, three times a day, after food. He is to leave for Florida, in a day or two, for a few weeks' change.

February 16th. The patient reports marked improvement since he arrived in Florida. His urine now averages 50 to 60 ounces daily, and he has gained 5 pounds in weight.

May 24th. The patient has just returned from Florida, where he spent three and a half months. Examination of his urine to-day shows it to contain 2 per cent. of sugar; no albumin present; quantity, 100 ounces. He was ordered codeia at bed-time, in $\frac{1}{2}$-grain doses, to be gradually increased, and to omit the arsenite of iron.

June 1st. No substantial improvement is apparent in the condition of the patient; in fact, he seems rather to be losing ground. It was, therefore, deemed wise to send him to the country to get him beyond reach of his business, since while in the city he could not be kept from dipping into commercial transactions, which made him very nervous. He was sent to Minnetonka for a

few weeks, with directions to follow closely the diet rules laid down, and to take no medicines.

September 1st. The patient has just returned to the city much improved by his two months' stay in the country. He reports that his urine was free from sugar a good deal of the time he was away. Examination of his urine to-day shows the specific gravity to be 1025, reaction acid, and entirely free from sugar and albumin.

September 20th. Sugar re-appeared in his urine in moderate quantity, owing largely to relaxation of his diet restrictions without orders.

November 11th. More or less sugar has been present in his urine since September 20th. The quantity of urine ranges from 80 to 100 ounces daily.

The patient concluded, upon his own responsibility, to go to California for the winter, where he died from diabetic coma almost immediately after his arrival.

The termination of the above case, under the circumstances, illustrates the dangers to diabetic patients of undertaking long journeys; the fatigues incident thereto so often precipitate diabetic coma. The patient derived much benefit from his residence in the country, but concluded, without my knowledge, to make the trip to California,—nearly three thousand miles by rail,—when he was not in condition to bear the fatigues of travel, and the result was as reported in the records.

Case 212, A. K.—*June 16, 1888.* Patient's age, 21 years; unmarried; apparently a very bright young woman. No family history of diabetes or tuberculosis is obtainable. She states that she was never seriously ill, except with scarlatina two years ago, until her present illness began. She states that about two years ago she

began to have unusual thirst, and to pass large quantities of urine; and she suffered much from weakness and a muscular lassitude. These symptoms were first noticed immediately after graduation from college, following a hard year's work in competing for a prize.

She consulted Dr. S., who found sugar in her urine, the quantity of the urine measuring 8 pints. The patient passed through the hands of several physicians, her condition being sometimes better, and at others worse, until the present date, when her symptoms were noted as follows: The quantity of urine averages 2½ to 3 quarts daily; she complains of much weakness; considerable thirst; is easily chilled; the throat and tongue are dry and red; she is rather nervous, and her menstrual flow has appeared but once during the last year. Her urine is pale, and rather green in color; its specific gravity marks 1038; its reaction is sharply acid, and it contains about 2½ per cent. of sugar. The urine is free from albumin.

The patient was directed to gradually restrict her diet to animal foods and green vegetables. No medicines ordered.

June 26th. The patient states that she feels less tired; that her thirst has sensibly diminished, and that the quantity of urine averages about 5 pints daily. Examination of the urine shows its specific gravity to be 1028, and to contain about 8 grains of sugar to the ounce. She was directed to draw the line very rigidly in the matter of diet—only taking meats and green vegetables, with eggs, and gelatin.

July 10th. Patient reports that the quantity of urine has measured from 3 to 5 pints daily since last visit. She has suffered from diarrhœa and more or less pain in her bowels during the last five days. The specific

gravity of the urine to-day is 1030, and it contains 6 grains of sugar to the ounce. She was directed to relax the diet restrictions somewhat for a few days, taking a small slice of bread twice daily, and she was ordered deodorized tincture of opium, 10 drops, after each loose movement of the bowels.

My absence abroad for three months necessitated referring the case to my colleague until my return.

October 30th. The patient reports as follows: Diarrhœa was present, more or less, for two or three weeks after last consultation. She has followed the diet rules advised faithfully up to date, and the quantity of the urine has not exceeded 4 pints daily. She now has no unusual thirst, no chills, and is very little tired, and she has gained a few pounds in weight. Her urine to-day, before breakfast, marks a specific gravity of 1035, and contains 7 grains of sugar to the ounce. After breakfast, sample shows specific gravity 1035, sugar 8 grains to the ounce. Patient's diet at present consists of meats, eggs, green vegetables, some cream. Ordered the same continued, excluding cream and adding almond-bread.

November 22d. Patient comes complaining of diarrhœa, distress in stomach, with flatulence, headache, some thirst. The urine is clear, color light; specific gravity, 1034; reaction acid; sugar present, 6 grains to the ounce. The urine is free from albumin.

As the almond-bread disagrees, she is to be permitted two or three small slices of common bread each day. To take 10 drops dilute nitromuriatic acid, with teaspoonful doses of pepsin-essence at meal-times.

February 8, 1889. The urine is clear; specific gravity, 1028; sugar, 6 grains to the ounce. Her stomach has been weak, more or less, since last visit, and some pain and flatulence present, but no diarrhœa. The urine has

averaged 3½ to 4 pints in quantity daily. Some days a little thirst has been present. She is to be permitted one apple a day, or one tomato, radishes, celery, green peas, and string-beans.

March 14th. The urine to-day is acid in reaction, clear, specific gravity 1029, and contains 5 grains of sugar to the ounce. The patient feels better; appetite is good; very little flatulence is now present. Treatment to be continued unchanged.

April 7th. The urine two hours after breakfast marks a specific gravity of 1029, and contains between 4 and 5 grains of sugar to the ounce. The daily volume of urine averages from 4 to 5 pints. The patient rises at night once to urinate. She was ordered to take 6 grains of lithium bromide an hour before retiring, as she has been somewhat sleepless of late.

May 17th. The urine has averaged from 3½ to 4 pints in daily volume since last consultation. The urine examined to-day, after breakfast, marked a specific gravity of 1023, and contained 3 grains of sugar to the ounce.

June 1st. Patient reports not having felt so well since last visit. She complains of pain in the top of her head; her stomach is disordered, and she suffers distress after food, with flatulence. Her bowels have been irregular, her tongue is coated, and she has disrelish for food, but she has no undue thirst. The daily volume of urine ranges from 3½ to 4 pints. Urine examined two hours after breakfast: specific gravity, 1021; sugar, about 1 grain to the ounce. The patient is following a closely restricted diet, consisting of meats, fish, eggs, gelatin, green vegetables, and occasionally a small slice of bread. No medicines.

July 9th. The volume of urine has ranged from 3 to 3½ pints daily since last consultation. The patient sleeps

much better,—in fact, better than for years; but her stomach is still weak. The urine to-day is acid in reaction, specific gravity 1026, and contains 2 grains of sugar to the ounce. The patient was sent to Waukesha for a few weeks to drink the waters.

September 3d. The patient returned from the springs about a week since, apparently improved. She states that she sleeps well; is not so easily tired; her appetite and digestion are much improved. The urine contains a small amount of sugar.

October 30th. Patient says she has not been so well since last visit, having had more or less trouble with her stomach. The urine to-day is clear, sharply acid in reaction, specific gravity 1028, and contains 8 grains of sugar to the ounce. Her gums are swollen and tender, and in places recede from the teeth. Very marked and typical *xanthoma* is present upon the lower and inner margins of both upper eyelids,—a condition claimed by some dermatologists to be associated very frequently with diabetes. The diet is maintained as strictly as possible according to the usual lines. No medicines save iron-wash for the mouth.

November 25th. The patient reports improved digestion, but the bowels have become rather costive. The mouth and gums are much improved under the use of iron-lotion. The urine marks a specific gravity of 1031, and contains 7 grains of sugar to the ounce.

December 12th. The patient states that she passes less urine of late; that she is very nervous and weak. She looks thin, and is evidently emaciating rather rapidly of late.

December 24th. Patient reports great disrelish for food, and complains of long-continued restrictions of diet. The urine is clear, acid in reaction, specific gravity

1026, and contains 5 grains of sugar to the ounce. The restrictions as to diet were largely removed, and the patient was put upon 10-grain doses of antipyrin, repeated three times daily.

December 28th. The urine marks a specific gravity of 1032, and contains 12 grains of sugar to the ounce. No change in diet was made, the patient to take whatever she chose except sugar and potatoes, and the antipyrin was increased to 45 grains a day.

December 31st. The urine marks a specific gravity of 1031, and contains 10 grains of sugar to the ounce, the volume of urine being about 5 pints daily. She has some thirst.

January 5, 1890. The urine marks a specific gravity of 1035, its reaction is acid, and contains 10 grains of sugar to the ounce. To continue antipyrin.

January 13th. The patient was suddenly seized during the night of the 11th with intense dyspnœa, vomiting, pain in her stomach, and collapse. Upon my visit she presented all the typical symptoms of diabetic coma, from which she died January 12th, at 10.50 P.M.

The above case well illustrates the worst type of the disease, as well as the difficulties to be encountered in the management of such cases. The patient was naturally a delicate woman, of nervo-sanguine temperament, the neurotic features being inherited from a pronouncedly hysterical mother. The chief obstacle in the way of successful treatment was her very delicate stomach, which could not be made to long tolerate the restrictions of diet essential to completely control the disease. When we consider that such cases usually run a rapid course, we must conclude that the treatment was not without influence in the above case, as the patient survived five years under the disease.

The next case belongs to the same class and type. The patient, however, possessed much better powers of digestion, and the result illustrates how much can occasionally be accomplished by treatment in the very worst type of the disease.

Case 194, G. S.—*February 10, 1888.* The patient comes from an adjoining State for advice about sugar in his urine. He states that his age is 18 years and 3 months. He began to be thirsty over a year ago, and about the same time he began to pass large quantities of urine. He experienced muscular weakness, and he found himself easily chilled. He relates that at one time he passed from 120 to 160 ounces of urine daily, and the specific gravity rose to 1050. His appetite became voracious. At 4 years of age he had diphtheria severely, but has suffered no serious illness since until the present disease appeared. He has been strong and hearty as a boy. No family history of diabetes could be traced. He was put upon a restricted diet by his family physician, at home, which modified his symptoms, although it did not eliminate the sugar from his urine. At present he seems well preserved, of healthy appearance, and the tendon reflexes are present in both legs. Examination of his urine showed it to be pale in color, clear, of acid reaction, specific gravity 1040, and to contain 15 grains of sugar to the ounce. The urine is free from albumin. He was ordered to gradually restrict his diet to meat, fish, eggs, gelatin, green vegetables, and a limited amount of bread, well toasted. No medicines were prescribed.

February 15th. The urine to-day marks a specific gravity of 1029, and contains 10 grains of sugar to the ounce. He has some constipation of the bowels and

headache; otherwise he is doing well. He has much less thirst, and does not rise at night to urinate.

March 1st. The urine marks a specific gravity of 1033, and contains about 7 grains of sugar to the ounce. The patient was directed to confine himself exclusively to animal food, not including milk.

March 15th. The patient has had considerable difficulty in accustoming his stomach to the restricted diet, as it has resulted in some pain and diarrhœa, although he is better to-day. The volume of urine for the last twenty-four hours was 64 ounces; its specific gravity is 1028, and it only contained about 1 grain of sugar to the ounce.

April 2d. The patient has suffered from pronounced diarrhœa with gastric pains for some days past; his bowels moved ten times yesterday. His urine marks a specific gravity of 1025, is free from sugar, and the volume for twenty-four hours past is 45 ounces. The urine contains a trace of albumin. He was permitted to relax slightly his diet restrictions, viz., to take one small slice of bread daily. To take tincture of opium, 8 drops, after each loose movement of the bowels.

April 5th. Patient looks pale, but he states that he feels better; his diarrhœa is much improved,—only one movement of the bowels yesterday. His urine averages from 45 to 50 ounces in volume daily; specific gravity, 1033; sugar, 3 grains to the ounce.

April 23d. Urine, to-day, specific gravity 1032; sugar, 5 grains to the ounce. Since last report there has been more or less diarrhœa, although he has been improving in that respect during the last week,—about two stools daily, unaccompanied by pain. He has suffered considerably from nausea, and he feels rather weak. Diet to consist of string-beans, cresses, some

milk, meats, tea, eggs, and a little bread. Ordered imported Carlsbad water to be taken three or four times daily.

May 8th. The urine has averaged from 44 to 46 ounces in volume daily. Patient says he feels "first-rate;" no weakness; stomach and bowels in good condition. The urine to-day is entirely free from sugar.

May 14th. Urine, 43 to 47 ounces daily; specific gravity, 1026; free from sugar.

May 21st. Urine to-day, 46 ounces; specific gravity, 1026; free from sugar. The patient's general condition has been improving. No weakness complained of; his digestion is good, but his bowels are slightly inclined to looseness. His diet to be practically limited to animal food.

June 2d. The urine averages from 40 to 52 ounces in volume daily. To-day the specific gravity of the urine is 1026, and sugar is absent. The patient continues well; no thirst, no diuresis, no weariness.

June 18th. Urine averages 43 to 45 ounces in volume; specific gravity, 1023 to 1027; no sugar. The urine has now been free from sugar, except occasional traces, for a month, and the patient has gained 10 pounds in weight. He is to leave for home in a few days, and is directed to continue strict diet, consisting of animal food with some selected green vegetables; no bread to be used.

January 7, 1889. The patient has returned to the city for treatment to-day. He relates that he is stronger than when he departed, in June; his stomach has given him little or no trouble, his bowels are regular, and there has been no essential change, so far as he is able to judge, although he has not measured his urine since June. His diet, while at home, has consisted chiefly of

animal food, with lettuce, string-beans, cabbage, eggs, and nuts. His urine to-day is clear, of acid reaction, specific gravity 1031, and contains about 7 grains of sugar to the ounce. He was directed to restrict his diet more closely to animal food.

January 14th. Urine, to-day, specific gravity 1028; reaction, acid; sugar, 5 grains to the ounce.

Februry 2d. Urine, to-day, specific gravity 1028; acid reaction; 3 grains of sugar to the ounce. As the quantity of sugar seems to fall no lower upon practically an animal diet, he was given codeine, $\frac{1}{4}$ grain at bed-time, to be slowly increased from day to day.

February 9th. The codeine causes some headache and nervousness, especially at night. His stomach remains in good condition. Urine, to-day, specific gravity 1026; sugar, 3 grains to the ounce. To continue codeine at bed-time, in doses of 1 grain and over.

February 16th. Patient states that his appetite has fallen off, and his bowels have become constipated; some flatulence is present, and he does not feel as well as usual. The quantity of urine has increased somewhat; specific gravity, 1031; sugar present, about 3 grains to the ounce. Codeine was omitted, and strychnia was ordered, in doses of $\frac{1}{30}$ grain, after meals.

February 23d. Urine, to-day, specific gravity 1026; reaction acid; sugar present, 4 grains to the ounce. No increase in volume of urine; no thirst; digestion improved. Treatment continued unchanged.

March 16th. Urine, to-day, specific gravity 1028; sugar, 2 grains to the ounce; patient feels "very well."

March 30th. Urine, to-day, specific gravity 1025; sugar, 2 grains to the ounce. The patient feels well, sleeps well, and has gained about 4 pounds in weight during the last two weeks.

April 20th. Urine specific gravity, 1026; sugar present in mere traces.

May 4th. Urine to-day, after luncheon, specific gravity 1026; sugar present in faint traces. Patient feels exceptionally well. Treatment unchanged.

May 11th. Urine, before breakfast, specific gravity 1022; entirely free from sugar. After breakfast, sample, specific gravity 1025; entirely free from sugar.

May 18th. Urine, to-day, specific gravity 1022; entirely free from sugar. The patient feels very well; his digestion is excellent; he sleeps well. The patient returns home with directions to live upon meats, fish, eggs, and gelatin. He was instructed to test his urine for sugar every week, and record the results.

December 1st. The patient reports that he has been doing excellently since he left the city, in May last. His urine has been free from sugar nearly all this time, until very recently, when he fell through the ice while skating, and became thoroughly chilled. Since then sugar has re-appeared in his urine in small amounts. He reports his general condition as better than for two years past, and that he is quite contented with his diet, which agrees with him admirably.

Cases of Mild Type.—The next 2 cases present precisely the opposite features from the preceding ones. They belong to a class in which the disease is almost invariably mild in character. For the most part these patients are between 45 and 75 years of age, usually well nourished, and have been rather generous in their habits of living, as well as active mentally and physically. If such patients can be induced to practice habits of moderate restriction of diet, it is usually a matter of no difficulty to eliminate the sugar from their urine, and to

maintain an excellent degree of general health, in which state they may continue almost indefinitely, without abridgment of the usual duties or comforts of life.

CASE 145, G. H.—*January 26, 1887.* The patient states that he is 61 years of age, and has heen an active business man all his life. He comes for advice in reference to thirst and diuresis, which he first noticed about a year ago. No family history of diabetes obtainable. He says that he has had great anxiety over his business affairs during the last two years. He rises at night to urinate very frequently; is thirsty, and very susceptible to cold. His appetite is very good; but he complains of being very nervous, and does not sleep well.

His urine examined to-day is light in color, clear, reaction sharply acid, specific gravity 1035, and contains 25 grains of sugar to the ounce. The urine contains a small percentage of albumin, and, upon microscopic examination, a few hyaline casts were observed.

Diagnosis.—Diabetes, complicated by contracting kidney (interstitial nephritis). He was directed to avoid potatoes and farinaceous foods, as well as fruits, and to take but little bread.

January 31st. The patient reports that he has less thirst; rises, at night, but once to urinate. Examination of his urine shows 12 grains of sugar to the ounce.

February 3d. The urine contains but 5 grains of sugar to the ounce. He was directed to live upon meats, green vegetables, and a small slice of bread twice daily, well toasted.

February 5th. Urine specific gravity, 1024; free from sugar.

February 15th. Urine, to-day, specific gravity 1021; no sugar present.

February 21st. The urine to-day is free from sugar, and the specific gravity is 1018. A small amount of albumin is still present in the urine.

March 3d. The urine to-day is free from sugar; specific gravity, 1016; a trace of albumin is present, and a few hyaline casts were observed upon microscopic examination.

The patient complains of weakness, and says he is very nervous. The drain upon his system, consequent to the disease for the last year, has evidently reduced him considerably. It was therefore deemed best to order rest for a time, and he was accordingly sent South, with directions to practice restrictions of diet to a moderate degree while absent.

April 9th. The patient has just returned from the South, greatly improved in general health. He states that he feels stronger, sleeps well, is not so nervous, and he looks much better. His urine is free from sugar; specific gravity, 1018; contains a trace of albumin and a few perfectly hyaline casts. He was permitted some relaxation in diet rules. In view of his interstitial nephritis, it seemed desirable to reduce his meat diet as much as possible, and to substitute therefor as much carbohydrates as possible, without causing sugar to re-appear in his urine. He was, therefore, allowed a medium amount of toasted bread, apples and tomatoes *ad libitum*, and nearly all vegetables, except potatoes, beets, and turnips. To substitute saccharin for sugar in sweetening his food and drinks. No medicines.

May 5th. Patient states that he feels very well; has attended to his usual business duties for the past month. His urine is free from sugar.

July 11th. Patient reports that he feels very well, has no thirst, is not nervous, sleeps well, etc. Examina-

tion of urine shows specific gravity 1020; free from sugar, but contains a small amount of albumin. He now lives upon his usual diet, except sugar and potatoes.

August 25th. Patient reports that he has been very well since last visit, and has gained considerably in weight. His urine to-day is free from sugar, specific gravity 1020, and a trace of albumin is present. He was permitted to throw off all restrictions of diet.

October 31st. Patient comes complaining of weakness in his limbs, tired feeling, and some nervousness. The urine contains about 4 grains of sugar to the ounce; its specific gravity is 1026. The unrestricted diet upon which he has lived for the last two months is evidently the cause of return of some of his diabetic symptoms. He was directed to avoid amylaceous and saccharine foods for the present.

November 28th. Urine to-day contains about 2 grains of sugar to the ounce; specific gravity, 1023.

January 31, 1888. The urine to-day is free from sugar, specific gravity 1014, and a trace of albumin is present.

March 13th. Urine is free from sugar; specific gravity, 1016. To continue moderate restrictions of diet.

May 16th. Urine is free from sugar; specific gravity, 1019. Patient states that he feels very well.

July 12th. The patient has been on rather a liberal diet for a month, and his urine again contains sugar—about 4 grains to the ounce. The specific gravity of his urine to-day is 1025, and a trace of albumin is present in his urine. He was directed to limit his diet more closely.

November 2d. Examination of urine shows specific gravity 1022; no sugar; a trace of albumin present,

and a few hyaline casts. He has been very well since last report, except for a week in August, when he suffered from slight diarrhœa.

December 20th. The urine contains a mere trace of sugar; specific gravity, 1021; some albumin is present.

January 10, 1889. The urine is free from sugar, and the patient feels well. The patient has now observed the effects of diet upon his urine so long and so closely that he can, as a rule, tell that which best agrees with him and that which will cause sugar to appear in his urine. He is able to use bread rather liberally,—3 to 5 ounces daily,—to eat strawberries, apples, tomatoes, and, in fact, nearly all table-vegetables except potatoes and farinaceæ, without causing his urine to become saccharine.

September 5th. Urine, to-day, specific gravity 1020, free from sugar; a trace of albumin present.

October 23d. Urine is free from sugar; specific gravity 1017; patient feels very well.

January 10, 1890. The urine is free from sugar, the specific gravity is 1022, and a small amount of albumin is present.

The above case illustrates how much can be accomplished by diet without medication in this class of cases. Upon moderately restricted diet no sugar is ever present in his urine. He is able to eat almost his usual amount of bread, and most vegetables except potatoes, rice, and farinaceæ; also to eat liberally such fruits as apples and strawberries without sugar appearing in his nrine. He has never, except in the beginning, been strictly dieted, because, in view of his contracting kidneys, it was deemed wise to permit as free use of vegetable foods as possible, short of causing sugar to appear in his urine. It will be noted that the specific gravity of his urine

frequently sank below 1020, and that on January 31, 1888, it even registered as low as 1014. It has already been pointed out that when granular kidney complicates diabetes, not only does the specific gravity of the urine often range low, but sugar may be present when the specific gravity is considerably below normal.

CASE 153, L. L.—*June 14, 1887.* Patient's age is 55 years. He states that he has always enjoyed good health, although he has lived liberally, taking more or less wine and spirits daily. He began to rise at night to urinate about two months ago. He finds himself weak and easily tired, is very sensitive to cold, and complains of much thirst. He states that his urine measures from 8 to 10 pints in volume daily. The urine marks a specific gravity of 1033, is acid in reaction, and contains 15 grains of sugar to the ounce. The urine is free from albumin. Potatoes, sugar, and farinaceous vegetables were prohibited, and bread was reduced to one-half the normal daily use.

June 28th. Patient reports that he feels somewhat better, though still weak. His urine contains 5 grains of sugar to the ounce; specific gravity, 1030; no albumin present.

July 12th. Urine specific gravity, 1020; acid in reaction; free from sugar and albumin. The patient was directed to live upon a moderately restricted diet, and to practice habits of temperance. His urine was examined a number of times subsequently and found to be free from sugar up to the end of the year.

I meet the patient frequently, and upon questioning him find no indications that sugar is present in his urine to date.

It would be easy to add numerous other cases from

my records here in which the disease proved mild and amenable to treatment in patients between 45 and 70 years of age. Such cases are to be met with daily in practice.

Case of Severe Type in Middle Age.—The following case is the most marked exception to the general rule laid down that I have ever encountered, and, since it is likely to prove of interest, I herewith transcribe it from my records in detail.

Case 185, Mrs. M.—*November 28, 1887.* Patient states that she is 47 years of age, married, and has had 10 children. She has had no serious illness until the present; no family history of diabetes obtainable. She states that her appetite and digestion have always been exceptionally good. She has had no special grief or worry or mental strain. No history of traumatism. She is not especially nervous. Her normal weight is 163 pounds; her present weight is 136 pounds. In January last—ten months ago—she first noticed that she was unusually thirsty, and that she arose frequently at night to urinate. She became much annoyed by a troublesome itching on the inner part of the thighs. These symptoms continuing, she consulted a physician, who discovered sugar in her urine, and ordered Giliford's solution of bromide of arsenic, which she took in gradually increasing doses until the present. Her daily dose now is 75 drops. Some restrictions in diet were also advised by her attending physician.

Her urine to-day is clear, of light-greenish color; reaction acid, specific gravity 1037, and contains 30 grains of sugar to the ounce. A trace of albumin is present, and the volume of urine is 10 pints in twenty-

four hours. She was directed to avoid potatoes, farinaceæ, saccharine foods, and to reduce her usual quantity of bread one-half. She was also ordered 6 grains of powdered jumbul after meals.

December 19th. Urine specific gravity, 1030; reaction acid; sugar, 20 grains to the ounce. The urine is free from albumin. Diet restrictions were drawn more closely, and jumbul continued as before.

January 9, 1888. The urine to-day marks a specific gravity of 1032, and contains 30 grains of sugar to the ounce. The patient was ordered codeine, beginning with ¼-grain doses after meals, to be increased daily. The dietary rules were drawn somewhat more firmly.

January 23d. Urine, to-day, specific gravity 1032; sugar present, 20 grains to the ounce; volume of urine for twenty-four hours, 6 pints. Codeine was increased to 2 grains a day.

January 31st. Urine specific gravity, 1030; sugar, 8 grains to the ounce. Codeine increased to 3 grains a day.

February 9th. Urine specific gravity, 1029; sugar present, 5 grains to the ounce. Codeine was ordered increased to 4 grains daily.

March 3d. Urine, to-day, specific gravity 1028; sugar present, 5 grains to the ounce. Diet to be limited to animal food, and codeine to be taken to the extent of 5 grains a day.

March 21st. Urine, to-day, specific gravity 1028; sugar, 3 grains to the ounce. The urine is free from albumin. The patient was obliged to discontinue the codeine on account of nausea, vomiting, constipation, and headache. She is to take no medicine for the present, but to live upon animal food.

April 21st. The urine, before breakfast to-day, has

a specific gravity of 1025, and contains 2 grains of sugar to the ounce. The patient has had some nausea during the last two weeks, otherwise she has felt better. Directions were given to relax the diet rules slightly for the present, as follows: To take some milk, oysters, lettuce, radishes, and 2 ounces of bread daily.

April 26th. Urine to-day marks a specific gravity of 1031, and contains 8 grains of sugar to the ounce. Volume of urine for twenty-four hours is 5 pints.

May 3d. Urine, to-day, specific gravity 1030; sugar, 6 grains to the ounce. Patient complains of weakness in her muscles; weary feeling; she is sensitive to cold, and has considerable thirst. She was ordered to discontinue the use of milk and bread, and confine her diet to meats, eggs, gelatin, and a few green vegetables.

May 23d. The urine marks a specific gravity of 1024, and contains 2½ grains of sugar to the ounce. Patient states that she feels much stronger and better generally.

June 4th. The urine averages 5 pints daily in volume. To-day the specific gravity is 1029, and the urine contains 5 grains of sugar to the ounce. The urine is free from albumin. The patient was ordered Clemens's solution of bromide of arsenic, to begin with 5-drop doses after meals, which is to be slowly increased.

June 28th. The patient complains of some thirst, is very tired much of the time. She states that her appetite is good. She is now taking 6 drops of Clemens's solution after her meals. Her urine to-day is as follows: Specific gravity, 1032; sugar, 7 grains to the ounce; no albumin present.

November 10th. The patient states that she has lost about 5 pounds in weight since last record. She now passes about 6 pints of urine daily; is thirsty at times, at others not. She states that she feels tired a good

deal of the time, but is never nervous. Urine, to-day, specific gravity 1028; reaction acid; sugar, 6 grains to the ounce; no albumin present. To eat fish, oysters, tomatoes, green vegetables, eggs, gelatin, cheese, and meats; also to eat almond-bread. To take no medicine for the present.

December 1st. The patient relishes the almond-bread very much; she is to continue diet as named unchanged. The urine, to-day, specific gravity 1030; sugar, 6 grains to the ounce.

December 17th. The urine has averaged 4 pints daily since last consultation. To-day examination of urine shows as follows: Specific gravity, 1026; sugar, 5 grains to the ounce. To continue diet as before, and to take ergotine (3 grains) after meals.

December 28th. The urine is about 5 pints in volume; specific gravity, 1029; sugar, 5 grains to the ounce. Ergotine to be increased to 5 grains after meals. No other change in treatment.

January 23, 1889. Patient states that the daily volume of urine is about 3½ pints. Urine, to-day, specific gravity 1027; sugar, 4 grains to the ounce. To discontinue ergotine, and to diet very strictly upon animal foods, taking, in addition, almond-bread only.

February 15th. The urine averages from 3 to 4 pints in volume daily. The specific gravity to-day is 1033, and the urine contains 3 grains of sugar to the ounce. The patient states that she has had considerable nausea, headache, and constipation of late. She was ordered strychnia, $\frac{1}{40}$ grain, with 10-drop doses of nitromuriatic acid, dil., after meals; the diet continued unchanged.

March 1st. Volume of urine has averaged 4 to 5 pints daily. Her appetite is still poor, although no nausea is present. The urine to-day is as follows: Spe-

cific gravity, 1030; sugar, 5 grains to the ounce. She was ordered morphine, $\frac{1}{4}$ grain at bed-time, to be slowly increased.

April 3d. The patient was obliged to discontinue the morphine on account of the nausea, headache, and constipation it induced. She was ordered, in place of the morphine, $\frac{1}{4}$ grain of nux-vomica extract with gentian. No essential changes in diet.

April 24th. Urine, to-day, specific gravity 1028; sugar, $2\frac{1}{2}$ grains to the ounce; volume, 4 pints. The patient was ordered strychnia, $\frac{1}{40}$ grain, after meals.

May 17th. The urine has averaged from $3\frac{1}{2}$ to 4 pints daily. Examination to-day as follows: Specific gravity, 1030; sugar, 2 grains to the ounce. Ordered strychnia increased to $\frac{1}{30}$ grain after meals. To diet strictly and to discontinue almond-bread.

June 1st. The patient states that she has no unusual thirst. She rises at night to urinate once each night. Her appetite and digestion are good, and she feels very well. The urine, to-day, specific gravity 1030; sugar, 3 grains to the ounce.

July 17th. Urine 4 pints in volume; specific gravity, 1028, acid reaction; sugar, 2 grains to the ounce. The patient was sent to Waukesha to drink the waters for a few weeks. She was permitted to use green vegetables while there.

September 26th. Patient has just returned from the Springs apparently improved in general condition. She was ordered an exclusively animal diet.

November 4th. Patient has had a cold for some days. She states that the urine has averaged from 5 to 6 pints daily. Some thirst is present. Urine specific gravity, 1027; sugar, 6 grains to the ounce. To take arsenite of iron, $\frac{1}{20}$ grain, after meals.

December 17th. Urine to-day is clear; acid in reaction; specific gravity, 1029; sugar, 6 grains to the ounce; no albumin; volume ranges from 5 to 6 pints. She was ordered nitro-glycerin, $\frac{1}{100}$ pill (McK. & R.), to be taken three times daily.

December 27th. Urine specific gravity, 1029; sugar, 8 grains to the ounce. Treatment to be continued, 5 pills of nitro-glycerin to be taken daily. No changes in diet.

January 4, 1890. Patient states that the volume of urine has ranged from 5 to 6 pints daily. Specific gravity of urine to-day is 1027; reaction acid; sugar, 6 grains to the ounce. The patient has some thirst.

She was ordered 15-grain doses of antipyrin three times daily, and to take green vegetables and one or two small slices of bread each day.

January 8th. Urine specific gravity, 1027; acid reaction; sugar, 4 grains to the ounce; no albumin. Patient complains of nausea, much of the time, since beginning antipyrin. To continue antipyrin, 45 grains daily.

January 16th. Urine specific gravity, 1028; sugar, 8 grains to the ounce. There has been no decrease in the volume of urine. To discontinue antipyrin.

January 25th. Urine specific gravity, 1026; acid reaction; sugar, 6 grains to the ounce; volume, 6 pints. Some thirst is present. The patient was again ordered an absolutely animal diet, mostly meats, fish, eggs, and gelatin.

February 12th. The patient notes no special changes. She has plainly fallen away in flesh during the last six months. Her skin looks wrinkled. She rises at night twice, on an average, to urinate, and the daily volume of urine is from 5 to 6 pints. Her gums are somewhat in-

flamed and tender. Urine specific gravity, 1029; sugar, 7½ grains to the ounc

It will be seen, from a review of the above record, that the patient, although over 50 years of age, suffers from the disease in the most obstinate form. The very strictest form of dieting has been enforced from time to time, and nearly every medicine resorted to of repute in such cases, without eliminating the sugar from the urine. The quantity of sugar has been greatly reduced, and maintained at a comparatively low range (about 1 per cent.), but it has never been entirely absent; the lowest point it ever reached was 2 grains to the ounce.

The patient has always had excellent digestive powers, and no nervous complication has been present. The disease has been very decidedly checked, and during the first two years' treatment it might be said to have been held fairly well under control. During the last six months, however, it is very plain that she is losing ground, and I have no doubt that a fatal termination of the case is not far distant.

With reference to the drugs employed in this case, codeine seemed to diminish to a slight degree the excretion of sugar when given in full doses; but ultimately codeine, as well as the other preparations of opium, had to be abandoned, because they induced nausea, headache, constipation, or other unpleasant after-effects.

Ergot for a time seemingly lowered the percentage of sugar in the urine to a slight degree, but ultimately it also disturbed the digestive organs. Antipyrin proved worse than useless, and, like in most other cases in my hands, it only did harm. On the whole, it will be perceived, from a close study of the case, that the patient did the best upon a restricted diet, with little or no medication.

Mild Type in Hebrew Patients.—It is pleasant to turn from such exceptionally intractable and unsatisfactory cases to another class in which the disease is usually mild and more amenable to treatment. It has already been pointed out that diabetes in the Hebrew race is nearly always mild and comparatively easily managed. The following cases are submitted as illustrations of that fact:—

Case 266, Mrs. A.—*October 15, 1889.* Patient's age is 44 years; inclined to stoutness; her mother and father were both diabetic. She states that in June last sugar was discovered in her urine; she also had much thirst and polyuria. She has recently suffered much from metrorrhagia, for which the uterus was curetted, but without relief, as she still has recurring hæmorrhages. She has practiced some restrictions of diet prescribed by her family physician. Examination of her urine to-day gives the following results: Specific gravity, 1028; reaction acid; sugar, 8 grains to the ounce. The urine is free from albumin. She has some thirst, and rises at night several times to urinate; she states that she feels very weak and easily chilled.

She was ordered to gradually restrict her food to meats, fish, green vegetables, eggs, gelatin, and to use no bread. No medicines were prescribed.

October 18th. Urine specific gravity, 1025; sharply acid; sugar, 4 grains to the ounce.

October 23d. Urine is clear; specific gravity, 1026; reaction acid; sugar, 2½ grains to the ounce; no albumin present. She was ordered to diet strictly upon meats and green vegetables.

November 2d. Urine to-day is clear; acid in reaction; specific gravity, 1021; entirely free from sugar and

albumin. Some uric-acid crystals of large size are present as urinary sediment.

November 12th. Urine to-day is clear; acid in reaction; specific gravity, 1023; free from sugar and albumin.

December 6th. Urine to-day is clear; acid in reaction; specific gravity, 1020; free from sugar and albumin. The patient states that she feels stronger and better in every way. Thirst has disappeared, and she no longer rises at night to urinate. She is to take one small slice of bread at her morning and evening meal,—2 ounces daily,—and more liberal use of vegetables is to be permitted, excluding potatoes, farinaceæ, and sugar.

December 28th. The urine to-day is clear; of acid reaction; specific gravity, 1024; free from sugar and albumin. To continue diet as before, unchanged.

January 20, 1890. The urine continues to be normal, and the patient is in good general condition, upon a moderately restricted diet. Her hæmorrhages have passed away, with the return of the urine to the normal condition.

Case 227, Mrs. L.—*February 9, 1889.* Patient's age, 54 years. She states that she has had sugar in her urine for over a year. At present thirst and diuresis is moderate in degree, as she has been dieting to some extent. Her back and shoulders are covered with small boils, which have been extremely painful and irritating for nearly three months. The urine is clear, of acid reaction, specific gravity 1027, and contains 10 grains of sugar to the ounce. The urine is free from albumin. She was directed to gradually restrict her diet to meats, fish, green vegetables, eggs, and gelatin, and to take one slice of bread morning and evening. She was ordered 10 grains of quinine daily in divided doses.

February 13th. Urine to-day clear; reaction acid; specific gravity, 1020; free from sugar.

February 23d. Urine, to-day, specific gravity 1025; a trace of sugar is present. The boils are rapidly disappearing. The patient was directed to discontinue the use of bread: otherwise to continue diet as before.

March 9th. Urine, to-day, specific gravity 1021; no sugar; no albumin. The boils have disappeared; but the patient complains of nervousness, for which bromide of lithium was ordered in 5-grain doses after meals.

March 19th. Urine to-day is clear; acid in reaction; specific gravity, 1021; no trace of sugar or albumin is to be found. The patient states that she feels excellently well, and is perfectly contented with the diet allowed. To discontinue lithium bromide and to continue diet as before.

June 21st. Urine to-day is clear; acid in reaction; specific gravity, 1020; perfectly free from sugar. The patient has continued perfectly well, her strength being entirely restored. No thirst, polyuria, or nervousness remain.

January, 1890. Urine, to-day, specific gravity 1020, acid in reaction, and absolutely free from sugar.

Case of Malarial Origin.—The next case is one of special interest as illustrating the occasional origin of diabetes in malaria, as the history of the case very clearly indicates:—

Case 135, C. W.—*June 5, 1885.* Patient's age, 54 years; a robust, strong-looking man; says that he has always lived regularly and temperately, but that he has had a good deal of exacting mental labor. He states that he has been under treatment for severe bronchitis

for a number of weeks past. He says that sugar was first discovered in his urine about two years ago. He was advised to practice some restrictions of diet, and to take arsenite of iron, which he thinks have done him some good. He states that he has suffered much from malarial attacks during the last twenty years. His malarial complications doubtless originated in Michigan, where much of his time has been spent in the forests as lumber-merchant. Examination of to-day's urine shows the following characters: Color light; reaction acid; specific gravity, 1035; sugar, 15 grains to the ounce; no albumin. He was directed to restrict his diet to meats, fish, green vegetables, eggs, gelatin, etc., and to take arsenite of iron, $\frac{1}{12}$ grain, after meals.

June 18th. The urine is free from sugar, and the patient goes East for a few weeks' rest.

November 8th. Urine, to-day, specific gravity 1036; sugar present, 10 grains to the ounce. The patient has been living upon unrestricted diet for some weeks past. He states that the use of quinine always benefits him. He says that without change of diet quinine lowers the specific gravity of his urine when it is unduly high. The patient was again instructed to regulate his diet and to take Giliford's solution of bromide of arsenic, in 10-drop doses, after his meals.

March 2, 1886. The patient has spent most of the winter on the Pacific coast, but was not especially benefited thereby. Had chills and fever while there and while traveling. He thinks he has had some sugar in his urine of late. Urine, to-day, specific gravity 1030; sugar present, 5 grains to the ounce. He was instructed to diet more closely, and to discontinue arsenic treatment.

May 3d. Urine specific gravity, 1025; no sugar.

The patient states that he rarely rises at night now to urinate, and that he feels very well.

June 13th. The urine is free from sugar, and the patient says he feels very well, except that he has some rheumatism. He was ordered to take sodium salicylate, 20 grains daily, for his rheumatism. No changes in diet.

July 6th. The urine is free from sugar. Rheumatism not much improved. He was ordered to continue lithium salicylate and warm baths. No change in diet.

July 12th. Urine specific gravity, 1025; no sugar present. Patient states that he feels better; his rheumatism is passing away. He is to continue the lithium salicylate.

July 19th. The patient states that the specific gravity of his urine has ranged, since last visit, at about 1020. He feels better than for three months past.

July 26th. The patient reports that he is free from rheumatism. His urine is free from sugar. He was directed to practice moderate restrictions of diet, and, for the present, to take no medicines.

August 20th. Urine, to-day, specific gravity 1023; free from sugar; contains no albumin.

October 25th. Urine, to-day, specific gravity 1018; free from sugar and albumin.

November 9th. Patient states that his urine has ranged, since last consultation, as follows: Specific gravity, 1016 to 1026; no sugar present. He states that he is feeling very well in all respects.

December 6th. Urine, to-day, specific gravity 1020; no sugar present.

February 3, 1887. Urine, to-day, specific gravity 1022; free from sugar. The patient was permitted to take a slice of white bread morning and evening, also to eat tomatoes; otherwise diet to be restricted to

meats, fish, green vegetables, gelatin, and eggs. No medicines prescribed.

March 22d. Urine, to-day, specific gravity 1024; free from sugar.

April 18th. Urine, to-day, specific gravity 1022; a faint trace of sugar is present. Patient complains of some rheumatism, for which he was ordered lithium salicylate, 5 grains three times daily.

May 5th. The specific gravity of the urine fluctuates much between 1014 and 1026. A slight trace of sugar is present in the urine to-day. Patient was ordered to continue lithium salicylate.

May 18th. Urine, to-day, specific gravity 1028; free from albumin, but contains 2 or 3 grains of sugar to the ounce. He was ordered Giliford's solution of bromide of arsenic, in 10-drop doses, after meals. The lithium salicylate to be discontinued.

July 11th. The patient states that he has been very well for the last month. Urine, to-day, specific gravity 1023; entirely free from sugar.

September 26th. Urine to-day is clear; acid in reaction; specific gravity, 1023; a trace of sugar is present. The patient has been allowed to indulge in fruits—peaches and apples—which he is now directed to discontinue. To continue Giliford's solution, as before.

November 5th. Urine to-day is clear; acid reaction; specific gravity, 1024; free from sugar. To continue treatment as before, unchanged.

March 20, 1888. The patient has just returned from New York, where he states he was not feeling well of late. For the past two or three days he has had acute cystitis, with some slight elevation of temperature. Urine to-day is cloudy; specific gravity, 1020; free from sugar; contains a large deposit of pus-corpuscles. He

was confined to his room, and put upon an infusion of triticum repens, with 10-grain doses of ammonium benzoate for his cystitis.

March 21st. Cystitis is not improved; patient urinates every hour, with pain and vesical tenesmus; some blood in the urine to-day. His temperature is 99.5° F. To take 12 grains of quinine daily, as malaria was suspected to be the cause of the elevation of temperature; triticum repens and ammonium benzoate to be continued as before.

March 24th. Cystitis continues more or less annoying; at times there is much pain in urinating. Urine to-day very cloudy; specific gravity, 1009; free from sugar; a small amount of albumin and a large amount of pus present. Treatment for cystitis continued unchanged, and quinine to be continued in the same doses as before. Diet restrictions to be somewhat relaxed.

March 30th. Urine very turbid still; specific gravity, 1011; free from sugar; considerable sediment of pus in urine still. There is much less distress from the cystitis to-day.

April 2d. Urine, to-day, specific gravity 1012; free from sugar, but very cloudy, and much sediment still. The lowered specific gravity of the urine is doubtless due to the large amount of demulcent drinks the patient takes for his cystitis.

April 20th. The patient has been very ill for the last three weeks. The cystitis was followed by remittent fever of almost malignant type, which refused to yield to quinine until the dose had been increased to 80 grains per day. Nothing short of 20-grain doses, repeated three or four times daily, seemed to have any modifying effect over his chills and elevated temperature. The patient is now much better in all respects.

May 5th. Urine, to-day, specific gravity 1030; sugar present, 7 grains to the ounce. The urine is increased in volume, but is now clear, and contains little or no pus.

As the re-appearance of sugar in the urine is doubtless due to relaxation of his diet rules, he is now directed to diet again strictly.

May 10th. Urine, to-day, specific gravity 1023; a trace of sugar is present—less than 1 grain to the ounce. The patient's general condition is improving very markedly. He was directed to take, once a week, 50 grains of quinine in divided doses during the day.

May 19th. Patient states that he is feeling stronger, and has gained somewhat in weight. Urine, to-day, specific gravity 1021; a trace of sugar is present.

May 21st. Urine, to-day, specific gravity 1021; sugar present, 2 grains to the ounce. The patient leaves for Carlsbad in a few days, to spend the season at the springs.

It should be stated that during the four years the patient has been under observation, he has suffered from attacks of chills and fever (malarial) about twice each year. Most of these attacks have occurred while he was absent from home. If he undertook a railway journey he was pretty sure to have an attack, an occurrence I have frequently observed in those who are saturated with malarial poison. His attacks have been comparatively mild, except the last one described in the records, complicated with cystitis.

Case Complicated by Amyloid Kidneys.—The next case is cited as illustrating an interesting but rather uncommon class of cases, in which diabetes becomes complicated with amyloid disease of the kidneys.

Perhaps, in the majority of such cases, as in the one to be related, diabetes is the complicating disease, the amyloid condition probably having existed for some time previous. The case also illustrates the relationship of tuberculosis to diabetes and amyloid conditions, which is not uncommon.

Case 102, J. W.—*February 17, 1880.*—The patient's age is 41 years, merchant, married; he states that he has been ill for six weeks, during which time he has lost 35 pounds in weight. He had a chronic cough some years ago, which was pronounced to be of tubercular origin by his physicians. He has not had syphilis. His left humerus is in a condition of chronic necrosis, discharging from several small openings, through which numerous small spicula of bone have been extruded at various times. At present only three openings are present, and very little discharge issues therefrom. He states that his necrosis is of about twenty years' standing. The three openings now discharging are situated just below his shoulder-joint; those lower down the shaft of the humerus have healed.

His present symptoms are great thirst, ravenous appetite, chills, much muscular weakness, dry skin, and pronounced diuresis; temperature, 97.5° F. He passes, by measure, from 16 to 18 pints of urine daily, which, upon examination, gives the following results: Specific gravity, 1028; acid reaction; clear; sugar, 20 grains to the ounce; a small amount of albumin is present, and a few large, clear casts were observed under the microscope. The patient was put upon an exclusive milk diet gradually enforced.

February 21st. Thirst is less urgent, and the urine is diminished in quantity; specific gravity, 1012.

March 3d. Urine specific gravity, 1012; some albumin present still.

March 10th. Patient has diarrhœa, and has vomited several times during the past two days. Urine, 5 pints; specific gravity, 1015. He states that he feels very weak and depressed, and that he does not sleep well. Slight œdema of left foot appeared for the first to-day. Albumin present in considerable quantity. Removed patient to hospital to-day for better care. Continued milk diet.

March 14th. The patient has had much nausea and some vomiting during the past two days. Urine contains about 6 grains of sugar to the ounce. To continue milk treatment for the present.

March 20th. Urine, to-day, specific gravity 1019; acid reaction; sugar present, 3 grains to the ounce; albumin, 15 per cent., bulk measure. Some granular and hyaline casts observed under the microscope.

March 31st. Urine, 4 pints in volume; specific gravity, 1014; a small amount of sugar present and considerable albumin. The bowels continue to be loose most of the time. The patient looks anæmic, and œdema is extending to the limbs and upper extremities. Patient was ordered to discontinue exclusive milk treatment, and to begin eating green vegetables, meats, fish, eggs, etc., still taking, however, a liberal quantity of milk with his other food.

April 10th. Dropsy is becoming general. Urine, 7 pints in volume; specific gravity, 1014; albumin, two-thirds, bulk measure; sugar, 4 grains to the ounce.

April 19th. Urine, 90 ounces; specific gravity, 1012; albumin, 45 per cent., bulk measure, upon standing twenty-four hours. Dropsy is becoming more marked daily. Patient was ordered dry hot-air baths, of half an hour's duration, each day.

April 25th. Urine, 160 ounces; specific gravity, 1012; albumin, 12 per cent., bulk.

April 30th. Urine, 192 ounces; specific gravity, 1010; albumin, 16 per cent., bulk measure; sugar present, 2 grains to the ounce. Dropsy is less marked. To continue diet and hot-air baths, unchanged.

May 4th. Urine, 224 ounces; specific gravity, 1009. Dropsy is subsiding rapidly under increased diuresis and diaphoresis, induced by hot baths.

May 8th. Urine, 12 pints; specific gravity, 1010; albumin, 20 per cent., bulk measure. The dropsy has almost entirely disappeared except in the feet. Patient feels very weak to-day. Hot bath was omitted.

May 17th. Urine, 6 pints; specific gravity, 1010; albumin, 36 per cent., bulk; sugar present, 2 or 3 grains to the ounce. A very obstinate diarrhœa has set in, which greatly weakens the patient. The stools are frequent and watery; the pulse is weak, and the extremities cold. Some sharp pain is complained of in region of the liver, and extending to right lung. These symptoms were followed by indications of collapse to-day. Deodorized tincture of opium was ordered in 15-drop doses, per rectum, after each loose stool. Restrictions of diet were removed, except as to sugar, potatoes, and farinaceæ.

May 21st. Urine, 5 pints; specific gravity, 1010; albumin, 30 per cent., bulk; sugar present, 4 or 5 grains to the ounce.

June 7th. Urine, 5 pints; specific gravity, 1009; albumin, 35 per cent., bulk measure; sugar present, 6 grains to the ounce. Dropsy is again becoming prominent, and diarrhœa is persistent. The liver and spleen are both considerably enlarged. The specific gravity of the urine descended to 1004 two days ago, but at this low gravity it contained *both albumin and sugar*, the

latter in very small amount—less than 2 grains to the ounce.

July 1st. The condition of the patient has fluctuated much for the last three weeks, but dropsy has been steadily increasing. The patient this morning passed into uræmia, and died during the night in comatose state without convulsions.

Cases Originating from Excessive Eating.—The next 2 cases are appended as types of that form of diabetes brought about by overingestion of food. That diabetes of severe grade is capable of being induced in certain individuals by intemperance in eating has already been pointed out in the section on Etiology. It only remains to bring forward clinical illustrations of such cases, as follow:—

Case 234, S. A.—*April 30, 1889.* Patient's age is 44 years; married; is a stout, robust-looking man; weight, 194 pounds; occupation, traveling salesman. He states that he was delicate as a child, but after 6 years of age he has had no illness. He has always had a good appetite,—indeed, too good; for, to use his own words, he "never knows when he has had enough to eat." He states that he uses tobacco and spirits moderately. He first noticed, a year or so ago, upon eating rapidly, that he vomited his breakfast occasionally, and this has become the rule of late. He began to be very thirsty four weeks ago, and to urinate very freely. His tongue became coated and dry, and he had headache much of the time. After two weeks or so, during which his symptoms grew more and more pronounced, he consulted a physician, who found sugar in his urine, and ordered a diet of mutton, veal, chicken, brown bread, and milk.

He states that he has been a great bread-eater, and that he has always taken a great deal of oatmeal with milk at his breakfasts. A sample of his urine which he brought for analysis contains a small percentage of sugar —about 2 grains to the ounce. He was directed to eat without restriction either as to quantity or quality of food for twenty-four hours, and then bring his urine for examination.

May 2d. Urine specific gravity, 1025; sugar, 4 grains to the ounce; no albumin. He was now directed to eat moderately; to stop the use of oatmeal, and to take little or no bread or farinaceæ; but, above all, not to overload his stomach.

May 6th. Urine of last evening, specific gravity, 1023; sugar present, but only a trace. He states that he has little or no thirst, and diuresis has diminished very decidedly; he no longer rises at night to urinate. He has not vomited for three days. He was ordered to continue diet as before, unchanged, and take no medicine.

May 13th. Urine specific gravity, 1020; absolutely free from sugar and albumin. The tongue has cleaned, thirst has subsided, diuresis has passed away, and no further nausea or vomiting has occurred.

June 1st. The patient states that he feels very well; has no thirst or polyuria. Urine specific gravity, 1020; free from sugar. He goes on the road for two months, with instructions to exclude from his diet farinaceæ, potatoes, and saccharine foods.

August 1st. Urine specific gravity, 1020; color normal; acid reaction; free from sugar and albumin. To continue treatment as before, unchanged.

October 2d. Urine, after breakfast of bread, eggs, and steak, specific gravity, 1021; acid reaction; free from sugar and albumin. He states that he never rises at

night to urinate now, has no thirst, is not weak; stomach is in excellent condition, and he sleeps well. He was permitted to eat apples and tomatoes, with bread, in moderation; in fact, diet to be very liberal in *quality*, but strictly moderate in *quantity*.

October 9th. The patient has been eating, for a week past, nine slices of white bread daily, and everything except sweets, potatoes, and farinaceæ. He has no thirst or diuresis.

Urine, to-day, specific gravity 1020; no sugar. To throw off all restrictions as to quality of diet except in the matter of sugar. He was especially instructed to eat moderately.

January 11, 1890. The patient states that he has been very well since last visit. He has no thirst; does not rise at night to urinate. He eats everything except sugar, "the same as before he took sick." Urine specific gravity, 1023; no sugar; no albumin.

He was directed to practice habits of temperance in eating, and to report if thirst or diuresis returns. There can be no doubt that in the above case diabetes was brought on by overloading the stomach. The patient was an enormous eater, for, as he frankly confessed, he "never knew when he had eaten enough." For nearly a year before sugar appeared in his urine he vomited his breakfast almost daily, and when he first came under observation he was suffering from the usual symptoms of food poisoning.

Case 282, H. B.—*December 7, 1889.* Patient's age 38 years; weight, 230 pounds; stout, plethoric man; comes for advice in reference to sugar in his urine, which was discovered yesterday by medical examiner for life-insurance company. His life was accepted three

years ago by another company. Preliminary examination of his urine shows it to contain 12 grains of sugar to the ounce; no albumin present. Patient states that he noticed thirst of late; he also says that he rises at night to urinate, passing large quantities of urine by night and by day. He has noticed considerable weakness, especially for the last sixty days or so. He states that he is a very large eater; has taken oatmeal very liberally for breakfast for the past fifteen or eighteen years. He eats his oatmeal with much sugar. He states that he is very fond of sweets. He does not eat much meat, but is very fond of bread and potatoes. He does not use spirits, but is a liberal tobacco-smoker. He suffers much from flatulence and eructations after meals. No history of diabetes is obtainable, either on his father's or mother's side of the family. Urine, to-day, specific gravity 1028; acid reaction; sugar present, 12 grains to the ounce. The urine contains no albumin. He was directed to avoid oatmeal, farinaceæ, sweets, etc., and to use bread in moderation. No medicines were prescribed.

December 12th. Urine, to-day, color normal; acid reaction; specific gravity, 1025; sugar, 3 grains to the ounce; no albumin.

December 19th. Urine, to-day, color normal; acid reaction; specific gravity, 1021; free from sugar. Patient feels greatly improved; is no longer weak; does not rise at night to urinate; is not thirsty. He was directed to use but little farinaceous foods and sweets, but especially to eat temperately, and to report any return of thirst or diuresis, especially if he rises at night to urinate.

March 4, 1890. Patient continues well, and his urine is free from sugar.

Case in Childhood.—The rarity of saccharine diabetes in childhood forms a sharp contrast with diabetes insipidus, so frequent in the early years of life. The following case, the youngest patient with diabetes whom I have treated, will illustrate both the severity and usually rapid course of the disease in subjects of tender age.

Case 223, B. G.—*December 31, 1888.* Patient's age, 4 years and 3 months. His mother first noticed in August last that he was urinating very frequently, "wetting the bed" at night. About the same time he became very thirsty. He has recently lost considerably in weight. He complains of being weak and tired much of the time. His mother states that he urinates about every half hour. Careful inquiry fails to reveal any history of diabetes in the family, but tuberculosis is prominent. The patient has had no serious illness before; but he fell upon the floor of a car a short time before his present illness begun, and sustained a severe blow upon his head. His urine to-day is clear; color light greenish-yellow; acid reaction; specific gravity, 1033; and contains 20 grains of sugar to the ounce. The urine is free from albumin. The patient was ordered a diet of milk, meats, a little cracker, and some green vegetables. No medicines were prescribed.

January 3, 1889. Urine, to-day, specific gravity 1025; sugar, 12 grains to the ounce.

February 4th. Urine specific gravity, 1030; sugar, 10 grains to the ounce; no albumin. Diuresis and thirst greatly diminished. He gives his nurse no more trouble at night from calls to urinate. The family physician now volunteered to cure the patient, and, as my prognosis was such as to afford the parents no hope of recovery, the patient passed into the hands of the more sanguine physician.

October 14, 1889. The parents of the child returned and requested me to resume treatment of the case. Examination of the patient disclosed extreme emaciation, great thirst, and diuresis. The patient had been permitted a mixed diet, including all fruits and farinaceæ, and, as a consequence, the disease had progressed at a rapid pace. Examination of the urine resulted as follows: Color light; reaction acid; specific gravity, 1038; sugar present, 25 grains to the ounce; urea, .013 gramme to cubic centimetre of urine; phosphates greatly in excess; the urine is free from albumin. The patient seems tired, weak, restless, and has little or no appetite. He was put upon milk, with a little bread; and quinine was ordered in 1-grain doses three times a day.

October 18th. The appetite has somewhat improved, and the patient seems less weak. The urine to-day is clear, acid in reaction, specific gravity 1033, and contains 25 grains of sugar to the ounce. Phosphates greatly in excess; no albumin present. Diet to be restricted almost entirely to milk. To continue quinine, 3 grains daily.

October 21st. Urine, 4 pints; specific gravity, 1029; sugar, 18 grains to the ounce. To continue treatment as before.

October 28th. The patient seems very weak, has little or no appetite. Urine, to-day, specific gravity 1033; sugar, 16 grains to the ounce; phosphates in excess; no albumin present.

November 4th. Urine, to-day, specific gravity 1029; clear; acid reaction; sugar present, 12 grains to the ounce; phosphates in excess. To continue milk diet, with very little bread, and some green vegetables.

November 12th. Urine specific gravity, 1024; acid reaction; sugar, 10 grains to the ounce. The patient is

weak, has little relish for food, and is troubled with slight cough.

November 24th. The cough is better, and, on the whole, the patient seems somewhat stronger. Urine, 5 pints; specific gravity, 1028; sugar, 10 grains to the ounce; no albumin.

December 6th. Urine is clear; color light; specific gravity, 1033; sugar, 10 grains to the ounce.

December 18th. Patient began to complain of pains in his stomach and bowels and to grow a little drowsy to-day. His respirations were somewhat quickened. He was given a hot bath, and hot bottles were applied to his extremities, and 10-grain doses of sodium bicarbonate were ordered every hour.

December 19th. Patient is more stupid to-day; sleeps much of the time. The respirations have increased in frequency to 40 per minute; the temperature is 101° F. The abdominal pains have subsided. Toward evening the patient became more stupid, and refused all food.

December 20th. Patient died to-day in a comatose state, without convulsions.

Cases Treated by Oxygen Inhalations.—The 2 following cases are herewith taken from my records of practice, more especially with the view of illustrating the oxygen treatment of the disease:—

Case 296, W.—*July 5, 1890.* Patient's age, 54 years; tall, dark, strong-looking man. States that he has had sugar in his urine, more or less, for four or five years. Last year he visited Carlsbad, and put himself under the care of one of the local physicians there for several weeks, with the result of considerable improve-

ment. Since his return home he has been dieting carefully, according to the instructions he received at Carlsbad. The patient's face, neck, and shoulders are covered with multiple boils, which he states have been gradually growing worse for the last six weeks, to his great annoyance. He rises at night to urinate, has slight thirst, some weariness of the muscular system. The urine is clear, specific gravity 1027, sharply acid, and contains 15 grains of sugar to the ounce; no albumin present.

Since his diet, as advised at Carlsbad,—which he is observing strictly,—seems proper, no essential changes were made in this respect, except to reduce his bread-allowance to 3 ounces daily, instead of 5 ounces, which has been his former allowance. Inhalations of pure oxygen gas were administered daily to the extent of 12 litres.

July 7th. The urine is clear, specific gravity 1030, reaction acid, and contains 12 grains of sugar to the ounce. No special improvement in the boils.

July 8th. Urine clear; acid in reaction; specific gravity, 1028; sugar, 8 grains to the ounce.

July 10th. Urine clear; color normal; reaction acid; specific gravity, 1027; sugar, 7 grains to the ounce. He was given 10 grains of quinine daily and oxygen inhalations continued as usual.

July 12th. Urine is clear; color normal; specific gravity, 1024; sugar, less than 2 grains to the ounce.

July 14th. Urine is clear; color normal; reaction acid; specific gravity, 1022; absolutely free from sugar. The boils are rapidly improving, and the patient states that he feels greatly improved.

July 20th. The urine to-day is clear; color normal; reaction acid; specific gravity, 1019; it is perfectly free from sugar. The boils have practically disappeared,

the thirst is gone, and the patient no longer rises at night to urinate. The oxygen inhalations were discontinued, and the patient was ordered to take glycozone (Ch. Marchand's) in teaspoonful doses before meals.

July 29th. The urine is clear; color normal; reaction acid; specific gravity, 1019; and perfectly free from sugar. The patient is, apparently, perfectly well, but was directed to continue the glycozone for the present.

August 16th. The urine is clear; color normal; specific gravity, 1022; reaction acid; quite free from sugar.

Case 298, H. B. P.—*June 15, 1890.* Patient's age, 47; weight, 210 pounds; tall, robust-looking; rather stout. He states that sugar was first discovered in his urine about five years ago. For the last three months he has had much thirst, and passes about 5 or 6 pints of urine daily. His digestion has been poor for five years or more. Bowels inclined to constipation. No hereditary history of diabetes. He recently returned from Carlsbad, where he went for the cure, and thinks he was much better while there. His urine to-day is clear; acid in reaction; specific gravity, 1027; it contains 24 grains of sugar to the ounce. No albumin present.

He was ordered inhalations of oxygen gas to the extent of 12 litres daily, and he was directed to limit his bread-allowance to 3 ounces daily.

June 18th. The urine is clear; color rather greenish; reaction acid; specific gravity, 1024; and contains 10 grains of sugar to the ounce. Patient states that his thirst has disappeared, that he does not rise at night to urinate, and that he passes but little more urine than normal. Oxygen inhalations to be continued as before, daily.

June 21st. The urine contains but 4 grains of sugar to the ounce to-day. Treatment to be continued as before.

June 24th. Urine to-day is clear; color normal; reaction acid; specific gravity, 1022; and perfectly free from sugar. Oxygen inhalations were ordered to be reduced to 6 litres per day.

June 30th. Urine is clear; color normal; reaction acid; specific gravity, 1020; absolutely free from sugar. Patient is to take 6 litres of oxygen every alternate day.

July 2d. Urine clear; color normal; reaction acid; specific gravity, 1020; no sugar.

July 11th. Urine to-day is clear; color normal; specific gravity, 1021; reaction acid; free from sugar.

July 17th. Urine clear; color normal; reaction acid; specific gravity, 1019; no sugar. Patient states that he feels perfectly well. He was ordered peroxide of hydrogen (Ch. Marchand's) in doses of 1 teaspoonful before meals in water, and the oxygen inhalations were discontinued.

The patient was directed to avoid saccharine and starchy foods, but was permitted 2½ ounces of common bread daily.

July 25th. Urine to-day is clear; color normal; specific gravity, 1020; free from sugar.

August 3d. Urine to-day clear; color normal; reaction acid; specific gravity, 1019; free from sugar. The patient goes to the sea-shore for a month with directions to continue the diet as laid down above, and to discontinue peroxide of hydrogen.

SECTION VIII.

Diabetes Insipidus

CLASSIFICATION.

Diabetes insipidus, polyuria, polydipsia, or hydruria, as the disease has been severally called, is a morbid condition of the system, the characteristic symptom of which is an excessive flow of urine of low specific gravity. As a rule, the urine contains neither albumin, sugar, or other morbid chemical products. Willis was the first to attempt a classification of the disease, and he described it under three divisions, as follow: (1) cases characterized by excessive excretion of aqueous urine, the solid matters being deficient—*hydruria;* (2) cases characterized by excessive flow of urine deficient in urea—*anazoturia;* (3) cases in which the flow of urine is excessive, and characterized by an abnormal quantity of urea—*azoturia.*

Parkes adopted a classification of the disease which had reference to the degree of tissue changes involved.

It seems more convenient and practical, as Dr. Ralfe has suggested, to adopt a classification which has reference, first, to the excessive excretion of water by the kidneys, and, second, to the increase of solids in the urine. *Hydruria* may be applied to cases characterized by excessive flow of aqueous urine, and *polyuria* to cases in which urea or other urinary solids are excreted in excess.

Our knowledge of the physiology of diabetes insipidus—meagre as it at present is—is largely due to the

investigations of Bernard. He has shown that the vasomotor centres for both the liver and kidney are comprised within the medulla oblongata. By experiments upon animals Bernard has shown that when the floor of the fourth ventricle of the brain in the central line is wounded the urine becomes saccharine and excessive in quantity. Wounded somewhat higher up, the urine becomes excessive in quantity, but contains no sugar. The higher area, therefore, comprises the vasomotor centre which presides over the kidney, while the lower area presides over the liver. Thus far, however, physiologists have failed to trace the path of the nervous influence from the vasomotor centre to the kidney, as has been done in the case of the liver.

ETIOLOGY.

Diabetes insipidus, like diabetes mellitus, is over twice more frequent in males that it is in females; but it differs from the saccharine disorder in its greater frequency in early life—most of the cases occurring under 30 years of age. It is quite common in childhood, and even in infancy, but the disease is rare in advanced life.

In a large proportion of the cases it seems impossible to clearly trace the disease to any definite cause. In a considerable number of cases, however, a distinct history of heredity is traceable. Lancereaux was able to trace about 15 per cent. of the cases to this cause. Diseases and traumatisms of the brain are, undoubtedly, frequent causes of diabetes insipidus. Lancereaux found about 16 per cent. of the cases to be due to this cause, while Roberts found a still larger percentage of cases originating from this source.

A considerable number of cases seem to owe their

origin to intemperance, especially to habitual alcoholic

The remaining causes assigned for the disease are: Exposure to cold, or sudden chills; drinking cold fluids when the body is overheated; hysterical and nervous conditions; mental emotion; acute inflammatory and febrile conditions. A cause which I do not remember to have seen recorded, but which I have more than once traced, is that of sexual excesses. The frequent micturition associated with irritable bladder, so common to excessive sexual indulgence, is not to be mistaken for polyuria. Finally, it is probable that nearly 40 per cent. of the cases of diabetes insipidus cannot be traced to any determinate cause.

PATHOLOGICAL ANATOMY.

The most frequent lesions found at the autopsy, in cases of diabetes insipidus, are those of the brain, although they are by no means uniform. From what has already been said of the physiology of polyuria, it is evident that any disease involving the higher area of the medulla oblongata is liable to give rise to this disease. Besides the various injuries to the head involving the cerebellar substance, it is not uncommon to find, at the autopsy, tubercular lesions implicating the upper medullar tract. More rarely syphilitic deposits have been found, as well as some of the hyperplastic growths. It is not absolutely essential that the primary lesion of the brain, which gives rise to diabetes insipidus, should be situated in the vasomotor centre for the kidney. Morbid growths or degenerative changes, elsewhere situated, may, by involving the circulation of or exerting pressure upon the renal vasomotor centre, bring about the disease secondarily. Miliary tuberculosis and

thickening have been found at the base of the brain in these cases, and in other localities not directly involving the fourth ventricle. With regard to the kidneys, the changes usually found are slight, and, for the most part, such as we might expect to find as a result of excessive functional activity of these organs, the most constant of these being hyperæmia and some enlargement. In those cases in which the disease has long continued, evidences of inflammatory action are frequent, and in some cases interstitial changes and atrophy are to be found. Dilatation of the bladder, ureters, and of the renal pelvis are common; and certainly their almost constant distention in these cases might be expected to bring about such results.

SYMPTOMS AND COURSE.

The most prominent symptoms of diabetes insipidus are diuresis and thirst. These are sometimes enormous, and they usually correspond closely in degree. Cases are commonly observed in which from 30 to 40 pints of urine are voided daily. Perhaps the largest quantity recorded was in a case related by Trousseau, in which the patient passed, during twenty-four hours, 56 pints of urine. Sir Wm. Roberts has recorded the case of a girl who passed more than a third of her weight of urine daily for several weeks. These, however, must be considered exceptional cases, ordinarily the range being from 10 to 30 pints daily. The urine is pale in color, almost watery in appearance, and usually of very low specific gravity, ranging from 1008 to 1002, and it may even descend lower. Notwithstanding this low specific gravity of the urine, and consequent disproportion of solids, the gross quantity of the latter eliminated by the kidneys may suffer no reduction whatever; indeed, the

quantity of urea and phosphates is often increased. The urine often contains *inosite*, but since this substance is often present during diuresis, however induced, it can scarcely be considered a morbid product, or at least one characteristic of this disease. In exceptional cases albumin or sugar may appear in the urine, especially in chronic and inveterate cases, but this is unusual.

Thirst is quite as prominent a symptom in diabetes insipidus as is diuresis; in fact, as already indicated, they usually go hand in hand together, the volume of fluid ingested corresponding closely with that eliminated. Some observers have claimed that the volume of urine exceeds the quantity of fluids imbibed in some of these cases; but more recent and accurate observations show that when the patient is unrestricted in the matter of drinks, the amount of fluid eliminated by the kidneys corresponds closely to that ingested. When the quantity of imbibed fluid is restricted, however, there seems to be some excess eliminated for a time, at the expense of dehydration of the tissues.

The thirst in diabetes insipidus is even more urgent than it is in diabetes mellitus, and, moreover, the capacity for fluids seems to be greater. There is this difference, however: in diabetes insipidus a copious draught usually satisfies the craving for water for a time, while in saccharine diabetes the thirst seems unquenchable.

In many of these cases the general health seems to be little, if any, impaired; more especially is this the case in that form of the disease termed *hydruria*, in which the elimination of solids is not excessive. Numerous cases are on record in which the disease has existed from childhood to middle and even advanced age, during all of which time the patients have

enjoyed a very fair degree of health and vigor, bodily and mentally. Indeed, it is recorded that some of the subjects of this disease have become fathers and mothers of large families, apparently suffering no discomforts or physical disadvantages except the frequent demands made by the system to ingest or void fluids. In other cases hydruric patients exhibit symptoms which correspond in a measure to a mild type of saccharine diabetes. Thus, more or less gastric discomfort may be experienced, often amounting to pain; the appetite may be morbidly increased, or again it may be impaired or abolished. The patient may become nervous, fretful, or querulous; and emaciation and general enfeeblement are sometimes the sequel in the more chronic cases. The abstraction of heat, caused by large quantities of fluids passing through the body, renders the patient susceptible to disagreeable sensations of cold, or to actual chills. The bowels are usually constipated, and sometimes this state alternates with attacks of diarrhœa.

In the *polyuric* form the general symptoms are apt to be most pronounced. The increased elimination of urea and phosphates point to retrograde tissue metamorphosis in progress, which sooner or later must tell upon both the vital and muscular forces. The quantity of urine, though greatly increased in this form of the disease, never reaches the enormous range common to hydruria. The specific gravity of the urine ranges usually from 1010 to 1025, and the reaction is distinctly acid.

Tessier has described certain of these cases, characterized by excessive quantities of phosphoric acid in the urine, under the name of "phosphatic diabetes." The essential features of these cases are slight, if any, increase in the volume of urine; but very decided increase

in the solids, especially of the phosphates. There is usually great debility, neuralgic pains, but moderate thirst, and the urine is of high specific gravity. Dr. Ralfe has confirmed Tessier's observations and recorded a number of similar cases.

The course of diabetes insipidus is exceedingly variable, depending much upon its cause. Thus, when brought about by diseases and traumatisms of the brain, its course is largely influenced by the extent and consequences thereof in each individual case.

As a rule, the disease is not directly fatal through its own effects. The loss of sleep consequent upon the frequent disturbance to urinate, or to quench thirst, coupled with mental worry and depression in delicate subjects, may at length bring about an enfeebled state of health, which often precipitates some secondary disease, from which the patient may succumb.

In the late stages of the disease œdema of the feet is common, and this is doubtless due to anæmia. Furunculæ (multiple boils) sometimes complicate this stage, although this is not so common as in diabetes mellitus.

The duration of the disease, as shown by the records, varies from a few months to fifty-nine years. The cases that recover usually do so within one or two years, although recoveries are recorded after the disease had lasted twenty years. In fatal cases death is most common within the first two years.

DIAGNOSIS.

Diabetes insipidus may be confounded with irritable bladder unless the symptoms are carefully distinguished. In irritable bladder the urine may be voided as frequently as in diabetes insipidus. Careful inquiry, however, will elicit the fact that the quantity of urine voided

is only an ounce or two at a time. Measurement of the twenty-four hours' urine will at once determine the point in question.

In granular atrophy of the kidneys (interstitial nephritis) the patient often rises at night and passes considerable quantities of urine of low specific gravity, with or without albumin. The quantity of urine, however, in these cases, if measured for the whole twenty-four hours, will usually be found only slightly to exceed the normal standard, and, moreover, the specific gravity rarely sinks so low as in diabetes insipidus. In granular kidney the polyuria occurs only—or chiefly—at night. Cardiovascular changes are usually present, and thirst is absent.

The absence of sugar from the urine distinguishes the disease from diabetes mellitus.

PROGNOSIS.

Diabetes insipidus may be regarded in general as a less serious disease than is diabetes mellitus; at the same time, it often resists all treatment, and runs a fatal course. In the hydruric form the disease is less fatal, though long continued, and absolute cure is the exception rather than the rule.

Cases arising in the wake of inflammatory diseases, or those beginning in youth without assignable cause, may be regarded as most favorable in a prognostic point of view.

In the polyuric form, which is attended by the loss of much solids by the urine, the prognosis must be looked upon as serious. Such cases are more apt to lay the foundation for some intercurrent disease, such as phthisis, or organic disease of the central nervous system, which precludes a favorable prognosis.

TREATMENT.

Experience has demonstrated that restrictions of food serve no useful purpose in this disease, and that restriction of drinks only do harm. It was thought, at one time, that the diuresis might be brought under control by limiting the amount of fluids ingested. This course not only greatly increased the suffering of the patient, but also, in at least one case, brought about a fatal termination through uræmia. The more advisable course is to permit the patient the use of water without restriction. In cases attended by excessive tissue metamorphosis—and they are the most numerous—the free ingestion of fluid serves to absorb and wash out the effete products, which must otherwise accumulate in the system, without doubt to the detriment of the latter. In addition to this the free use of fluids relieves the chief discomfort of the patient—his thirst; and we have no right to deny him this relief through measures that are, in themselves, harmless. The patient may, therefore, indulge in aqueous beverages *ad libitum*, and he will find lemonade, especially if made with soda-water, very grateful to the palate. Alcoholic drinks increase both the thirst and diuresis, by abstracting water from the tissues, and, therefore, they should be avoided. The patient should not take his beverages too cold (iced),—an injunction not to be overlooked, as he is sure to select iced drinks, if not otherwise instructed.

The patient should be warmly clad; pure-wool garments should be worn next the skin at all times. With a view to relieve the tension of the visceral circulation, which favors diuresis, warm baths should be employed, as they invite the blood to the surface and prove very serviceable. The good effects of warm baths are ren-

dered more durable by following them with thorough frictions of the skin by means of coarse towels.

Of the medicinal agents employed for the relief of diabetes insipidus, *ergot* seems to have enjoyed the highest as well as the longest popularity in point of time. On theoretical grounds, the indications for the use of ergot are clear. Its contractile power over the small vessels should lessen the blood-tension in the renal circulation, and thus lessen the excessive diuresis. In some cases the drug undoubtedly exercises a favorable influence over the disease, as a number of unquestionable cures have been effected by it. It is somewhat uncertain, however, in its effects, many cases failing to improve under its use. It should be employed in full doses in order to be effective—℥i to ℥ii of the fluid extract (preferably Squibb's).

Valerian was long ago recommended by Trousseau for diabetes insipidus. Both he and Rayer claimed the very highest merit for large doses of this drug; but these claims have scarcely been realized by its subsequent use.

Opium seems to diminish the diuresis in some cases, but in others it only aggravates the symptoms, and, on the whole, the evidence does not favor its employment in these cases. The same may be said of belladonna.

Various other drugs have been recommended for diabetes insipidus, among which are *acetate of lead*, *arsenic*, *the bromides*, *camphor*, *jaborandi*, etc. The only one of these that I have derived good results from has been the bromide compounds, especially the bromide of sodium. In at least two cases of recent origin I believe the disease was arrested by full doses of sodium bromide. To be effective the dose should be rather large. The patient should be rapidly brought under its influ-

ence by the administration of from 2 to 4 drachms during the first twenty-four hours; after that, 20 to 30 grains should be given every four to six hours, until some muscular relaxation in the legs is noted, or slight unsteadiness in walking. After the above effects are obtained, the dose should be decreased to a point just short of affecting the locomotion. The constant galvanic current has been found beneficial in some cases. The best results are said to follow the application of the positive pole to the cervical region over the vertebra and the negative pole to the lumbar region and pit of the stomach, alternately.

Antipyrin has recently been brought forward as a remedy for diabetes insipidus, and several cures are recorded from its use. The dose recommended is from 2 to 5 grammes daily. In the polyuric form of the disease, where the loss of solids by the urine is excessive, an effort should be made to conserve the tissue waste by tonic medication. Among the most useful agents of this class will be found *strychnia*, *iron*, *quinine*, and *arsenic*. In cases in which the disease is traceable to traumatic lesions of the brain, intra-cranial growths, constitutional taints, etc., the treatment should include appropriate measures for the relief of the primary disease.

BIBLIOGRAPHY.

It has been found absolutely necessary to limit the following list to treatises on the subject. The large mass of current literature on diabetes, if included, would occupy altogether too much space in a volume of this size.

Aenstools, F. Zur Etiologie und Symptomatologie des Diabetes Mellitus. 8vo. Griefswald, 1869.

Andrey. Du Diabète et de son Traitement. 4to. Paris, 1869.

Auch, F. G. De Diabete. 8vo. Berlin, 1835.

Auffan, A. Du Diabète Sucré ou de la Glucosurie. 4to. Strasbourg, 1859.

Bandelow, E. De Diabete Mellito. 8vo. Berlin, 1838.

Barnaud, A. Du Diabète Sucré. 8vo. Berne, 1862.

Barow, F. De la Glucosurie ou Diabète Sucré. 4to. Paris, 1853.

Bell, H. An Essay on Diabetes. 8vo. Transl. London, 1842.

Burnett, J. B. Diabetes Mellitus. 8vo. Edinburgh, 1801.

Bennighof, J. P. Ueber Melliturie. 8vo. Munich, 1843.

Bernard, C. Leçons sur le Diabète et la Glycogenèse Animale. 8vo. Paris, 1877.

Bertail, E. Étude sur la Pthisie Diabètique. 4to. Paris, 1873.

Biaille-Lalongeay, J. B. A. A. Du Diabète Sucré, et specialement de ses rapports avec les differents modes d'alimentations. 4to. Paris, 1848.

Bibergeil, H. On Diabetes Mellitus. 8vo. Berlin, 1835.

Biggs, B. E. Diabetes Mellitus. 8vo. Edinburgh, 1803.

Bos, J. J. Bijdrage tot de kennis der Glycogenese bij den Diabetes Mellitus. 8vo. Amsterdam, 1867.

Brandao, A. B. de S. Glycosuria. 4to. Bahia, 1871.

Brigham, C. B. Diabetes Mellitus. 8vo. Boston, 1868.

Brouwer, N. Akademisch procfschrift over den Diabetes Mellitus. 8vo. Groningen, 1862.

Budde, T. De Diabete Mellito. 8vo. Gryphie, 1835.

Champlin, J. M. On Diabetes and its Successful Treatment. 8vo. From second London edition. New York, 1861.

Capezzuoli, S. Sul Diabete. 8vo. Florence, 1851.

Carter, C. De Diabete Mellito. 4to. Paris, 1811.

Cazalas, L. Du Diabète. 4to. Montpellier, 1875.

Chaloin, L. E. Du Diabète Sucré. 4to. Paris, 1853.

Cludius, O. C. De Diabete qui dicetur Mellitus quædam. 8vo. Regimonte, 1843.

Contour, L. A. Du Diabète Sucré. 4to. Paris, 1844.

Currie, F. On Diabetes. 8vo. Edinburgh, 1798.

Cyr, J. Etiologie et Pronostic de la Glycosurie et du Diabète. 8vo. Paris, 1879.
Dantagnan, E. M. Étudie Physiologique sur la Glycosurie. 4to. Paris, 1866.
Dedebaut, J. P. L. Du Diabète Sucré. 4to. Paris, 1856.
Destouches, A. A. Du Diabète Sucré. 4to. Paris, 1817.
Dickinson, W. H. Diseases of the Kidneys and Urinary Derangements. Part I, Diabetes. 8vo. London, 1875.
Diehl, G. Butrage zur Pathologie und Therapie des Diabetes Mellitus. 8vo. Erlangen, 1875.
Donkin, A. S. The Skim-Milk Treatment of Diabetes and Bright's Disease. 12mo. London, 1871.
Driessen, J. C. De Phosphuria et Diabete Mellito. 8vo. Groningen, 1818.
During, A. von. Ursache und Heilung des Diabetes Mellitus. 8vo. Hannover, 1868.
Dumoulin, A. Considerations sur la Pathogènie et sur le Traitement du Diabète. 8vo. Lousle-Saulnier, 1877.
Dupla, A. Du Diabète Sucré. 4to. Paris, 1864.
Duport, S. F. E. De la Glucosurie ou Diabète Sucré. 4to. Paris, 1853.
Duquesnal, P. J. Sur le Diabète Sucré. 4to. Paris, 1816.
Dusseaux, L. J. F. Sur le Diabète. 4to. Paris, 1835.
Dyett, R. H. Diabetes Mellitus. 8vo. Edinburgh, 1808.
Dzondi, C. H. Diabetes natura Oculi Pathologia Illustratur. 8vo. Halis, Saxony, 1830.
Eckholt, D. De Diabète. 4to. Argentorati, 1863.
Ehrmann, J. Die Honigartige Harnruhr. 8vo. Wurzburg, 1830.
Eichelbaum, M. De Diabete Mellito. 8vo. Berlin, 1848.
Ellebrecht, A. Ueber Diabetes Mellitus. 8vo. Bonn, 1880.
Elliott, J. On Diabetes Mellitus. 8vo. Edinburgh, 1802.
Erhard, C. J. Ueber Diabetes Mellitus. 8vo. Wurzburg, 1862.
Erskine, P. On Diabetes. 8vo. Edinburgh, 1801.
Esser, P. Ueber Diabetes Mellitus. 8vo. Bonn, 1869.
Ellenger, N. von. Diabetes Mellitus. 8vo. Berlin, 1868.
Evans, L. Diabetes Mellitus. 8vo. Edinburgh, 1805.
Fanninger, F. De Diabete Mellito. 8vo. Berlin, 1820.
Feith, E. Physiologico-Pathologica de Diabete Mellito Commentatio. 8vo. Berlin, 1861.
Filkin, T. Diabetes Mellitus and its Complications. 8vo. Edinburgh, 1821.
Fischer, C. De Mellituria. 8vo. Berlin, 1867.
Fitzgerald, J. On Diabetes. 8vo. Edinburgh, 1800.
Fock, F. De Diabete. 8vo. Berlin, 1839.
Forstmann, G. De Diabete. 8vo. Berlin, 1839.
Franke, H. Ueber die Heilbaskeit des Diabetes Mellitus. 8vo. Halle, 1873.
Friedel, L. A. F. De Diabete. 8vo. Berlin, 1839.
Froning, F. Versuche zum Diabetes Mellitus bei Ischias. 8vo. Gottingen, 1879.
Fullerton, R. On Diabetes. 8vo. Edinburgh, 1827.
Gaehtgens, C. Ueber den Stoffwecksel eines Diabetikers verglichen mit dem eines Gesunden. 8vo. Dorpat, 1866.

Gaillard-Bournazel, J. De la Glycosurie ou Diabète Sucré. 4to. Paris, 1856.
Gantz, J. C. V. De Diabete. 4to. Jena, 1770.
Garnier, E. De la Glucosurie ou Diabète Sucré. 4to. Paris, 1858.
Gaulard, L. De la Glucosurie. 4to. Paris, 1871.
Georgeon, J. B. Du Diabète Sucré. 4to. Paris, 1843.
Gley, F. F. De Diabete Mellito ejusque Medela. 4to. Jena, 1829.
Glogowski, F. De Mellituria. 8vo. Dorpat, 1854.
Grant, J. Diabetes. 8vo. Edinburgh, 1821.
Grohmann, J. F. R. De Diabete. 4to. Leipsic, 1808.
Gross, G. Ueber die Zuckerharnruhr. 8vo. Munich, 1862.
Grosse, C. A. De Diabete. 4to. Leipsic, 1806.
Gunzler, A. Ueber Diabetes Mellitus. Small 8vo. Tubingen, 1856.
Haering, C. H. H. A. Einige Boebachtungen ueber Diabetes Mellitus. 4to. Kiel, 1869.
Haenslmair, J. B. De Diabete. 8vo. Monachii, 1832.
Hall, G. Diabetes. 8vo. Edinburgh, 1794.
Harley, G. Diabetes: its Various Forms and Treatment. 8vo. London, 1866.
Harvey, J. Diabetes Mellitus. 8vo. Edinburgh, 1820.
Heidenreich, F. A. Observationes quædam institutæ in tribus Diabetices. 8vo. Regimonti Pr., 1844.
Heinemann, J. G. De Dyscrasia Saccharina. 4to. Argentorati, 1843.
Helfreich, F. C. Ueber die Pathologenese des Diabetes Mellitus. 8vo. Wurzburg, 1866.
Hobelmann, P. Ueber die Harnruhr. 8vo. Wurzburg, 1834.
Hohlfeld, R. De Diabete Mellito. 8vo. Berlin, 1828.
Huelsmann, C. J. De Diabete. 8vo. Berlin, 1837.
Hunseler, P. Ueber Diabetes Mellitus. 8vo. Bonn, 1867.
Huld, F. C. L. De Diabete Mellito. 8vo. Berlin, 1867.
Hulme, J. On Diabetes Mellitus. 8vo. Edinburgh, 1798.
Hummel, M. Ueber Diabetes Mellitus. 8vo. Munich, 1849.
Jall, E. De Diabete. 8vo. Monachii, 1834.
Jangot, C. M. De la Théorie du Diabète Sucré. 4to. Paris, 1851.
Jansen, F. De Diabete. 8vo. Gryphia, 1833.
Kalinowski. Du Diabète Sucré. 4to. Paris, 1866.
Karth, J. De Dyscrasia Saccharina. 8vo. Bonn, 1840.
Klawilter, R. De Diabete Mellito. 8vo. Gryphia, 1863.
Koch, E. Ueber Diabetes Mellitus. 8vo. Jena, 1867.
Koesen, G. E. De Diabete. 4to. 1767.
Korseck, C. De Diabete. 8vo. Berlin, 1840.
Krause, J. G. A. Annotationes ad Diabeten. 8vo. Halle, 1853.
Kraussold, H. Zur Pathologie und Therapie des Diabetes Mellitus. 8vo. Erlangen, 1874.
Kuntzel, P. Experimentille Butrage zur Lehre von der Melliturie. 8vo. Berlin, 1872.
Kuester, E. De Diabete Mellito. 8vo. Berlin, 1863.
Kuse, H. De Diabete Mellito. 8vo. Berlin, 1865.
Labosse, J. B. De la Glucosurie. 4to. Paris, 1853.
Laffont, M. Recherches sur la Glucosurie Considérée dans ses rapports avec le système nerveux. 4to. Paris, 1860.

Lallier, H. Discussion sur la nature du Diabète Sucré. 4to. Paris, 1853.
Lammergelle, T. W. De Diabete. 4to. Jena, 1717.
Landau, T. A. Théorie et Traitement de la Glycosurie. 4to. Paris, 1868.
Lankers, A. De Diabete. 4to. Lugd Bat, 1720.
Latham, J. Facts and Opinions Concerning Diabetes. 8vo. London, 1811.
Lecorché. Traité du Diabète Sucré, Diabète Insipidi. 8vo. Paris, 1877.
Lefèvere, E. A. Du Diabète Sucré. 4to. Paris, 1822.
Leow, A. De Diabete Mellito. 8vo. Berlin, 1849.
Letellier, J. A. L. T. Sur le Diabète. 4to. Strasbourg, 1823.
Level, J. Des Symptomes des Diabètes. 4to. Paris, 1841.
Liman, C. L. C. De Diabete Mellito. 8vo. Hallis, 1842.
Limberg, D. De Diabete. Small 8vo. Heidelberg, 1737.
Lindner, J. De Diabete. Monachii. 8vo. 1810.
Lynch, J. C. Diabetes Mellitus. 8vo. Edinburgh, 1804.
Maillard, R. P. M. Sur le Diabètes Sucré. 4to. Paris, 1804.
Malloch, J. M. G. On Diabetes Mellitus. 8vo. Edinburgh, 1808.
Mann, A. Diabetes Mellitus. 8vo. Edinburgh, 1785.
Maracet, A. On Diabetes. 8vo. Edinburgh, 1797.
Mariani, T. De la Glucosurie ou Diabète Sucré. 4to. Paris, 1867.
Meisenberg, C. De Diabete Mellito. 8vo. Bonn, 1865.
Mensert, H. M. De Diabete. 8vo. Amsterdam, 1841.
Merekel, A. E. E. Nonulla de Diabete Mellito. 12mo. Dorpat, 1835.
Mettegang, L. De Diabete Præsertim Mellito. 8vo. Berlin, 1838.
Michaelis, T. De Diabete Mellito. 8vo. Berlin, 1838.
Michels, W. Ueber Diabetes. 8vo. Berlin, 1868.
Mueller, E. De Diabete. 8vo. Berlin, 1845.
Mueller, G. L. De Diabete Præsertim Mellito. 8vo. Gottingen, 1822.
Myers, J. H. On Diabetes. 8vo. Edinburgh, 1779.
Nicolai, E. A. De Diabete. 4to. Jena, 1770.
Noeller, E. De Diabetæ Melliti Natura. 8vo. Berlin, 1848.
Nurnberger, G. T. Die Zuckerharnruhr. 8vo. Berlin, 1867.
Olivier, R. J. L. B. Du Diabète Sucré. 4to. Paris, 1859.
Oltendorf, M. De Diabete Mellito. 8vo. Berlin, 1833.
Pellasin, C. J. Du Diabète Sucré. 4to. Paris, 1853.
Pilting, T. De Diabete Mellito. 8vo. Jena, 1851.
Plass, H. L. Ueber die Wahre Harnruhr. 8vo. Wurzburg, 1838.
Planter, E. F. De Diabete Mellito cum Lithiasé Comparando. 8vo. Leipsic, 1835.
Prout, W. Nature and Treatment of Diabetes, Calculus, etc. 2d ed. London, 1825.
Raben, C. De Diabete Mellito. 12mo. Havnie, 1806.
Ranke, A. De Diabete Mellito. 8vo. Berlin, 1854.
Reemelin, R. Ueber Diabetes Mellitus. 8vo. Wurzburg, 1875.
Reich, F. T. De Diabete Mellito Questiones. 8vo. Gryphie, 1859.
Reichard, J. De Diabete Mellito. 8vo. Pestini, 1834.
Rhode, L. Ueber Diabetes Mellitus. 8vo. Wurzburg, 1880.
Robagila, S. Du Diabète Sucré. 4to. Paris, 1849.
Robertson, A. J. On Simple Diabetes Mellitus. 8vo. Edinburgh, 1820.
Rochabrun, C. E. Du Diabete. 4to. Paris, 1849.

Rollo, J. An Account of Two Cases of Diabetes Mellitus, to which are added a general view of the nature of the disease, and its appropriate treatment. Vol. ii, 8vo. London, 1797.
Rouquier, T. Sur le Diabetes. 8vo. Paris, 1808.
Ruickoldt, A. Ein Beitrag zur lehre von der Zuckerharnruhr. 8vo. Jena, 1865.
Ryan, R. On Diabetes Mellitus. 8vo. Edinburgh, 1799.
Salomon, D. De Diabete Mellito. 8vo. Gottingen, 1808.
Saloy, A. C. Du Diabète Sucré. 4to. Paris, 1861.
Sarran, L. Du Diabète Sucré et de son Traitement. 4to. Paris, 1865.
Sauberg, G. A. De Diabete Mellito. 8vo. Berlin, 1865.
Scharlau, G. W. Die Zuckerharnruhr. 8vo. Berlin, 1846.
Schnee, E. Diabetes and its Treatment. American transiation. Small 8vo. Philadelphia, 1889.
Schenck, F. L. De Diabete Mellito Pathologia. 8vo. Berlin, 1841.
Schmidt, A. T. De Diabete Mellito. 8vo. Halis Sax, 1844.
Schultz, E. Ueber Diabetes Mellitus. 8vo. Halle, 1868.
Schwerin, M. De Diabete Mellito Nonulla. 8vo. Berlin, 1839.
Schulfort, T. P. Du Diabete. 4to. Strasbourg, 1858.
Seegen, J. Der Diabetes Mellitus auf Grundlage Zahlreicher Beobachlungen Dargestellt. 8vo. Leipsic, 1870.
Seelmair, B. Ueber das Wesen der Zuckerharnruhr. 8vo. Munich, 1859.
Seyfried, R. De Diabete. 8vo. Berlin, 1849.
Shirreff, J. H. On Diabetes Mellitus. 8vo. Edinburgh, 1804.
Shuter, J. Diabetes Mellitus. 8vo. Edinburgh, 1800.
Siegmayer, J. C. G. De Diabete. 8vo. Berlin, 1827.
Siemssen, F. C. A. De Diabete. 8vo. Halæ, 1828.
Smith, A. H. Diabetes Mellitus and Insipidus. 12mo. Detroit, 1889.
Spieker, R. De Diabete. 8vo. Berlin, 1839.
Spieseke, A. R. De Diabete Mellito. 8vo. Berlin, 1865.
Stevenson, G. On Diabetes. 8vo. Edinburgh, 1762.
Strauss, G. D. F. Die Einfache Zuckerlose Harnruhr. 8vo. Tubigen, 1870.
Streppel, C. De Diabete Mellito. 8vo. Berlin, 1867.
Thilloy, H. E. Du Diabète. 4to. Paris, 1852.
Tyson, J. A Treatise on Bright's Disease and Diabetes. 8vo. Philadelphia, 1881.
Ueberhorst, R. De Diabete Millito Nonulla. 8vo. Berlin, 1841.
Ullrich, F. Sur le Diabète. 4to. Paris, 1879.
Vayssiè, P. C. Du Diabète Sucré. 4to. Paris, 1848.
Vernon, N. On Diabetes. 8vo. Edinburgh, 1796.
Volkmann, J. F. T. De Diabete Mellito. 8vo. Regemonto Pr., 1849.
Wandner, G. Die Zuckerige Harnruhr. 8vo. Regensburg, 1859.
Washington, W. An Essay on the Disease Commonly Called Diabetes. 8vo. Philadelphia, 1802.
Weber, G. De Diabete Mellito. 8vo. Berlin, 1865.
Wunnenberg, L. Ueber Diabetes Mellitus. 8vo. Bonn, 1870.
Zabel, C. A. De Diabete Mellito. 8vo. Halis, 1858.
Zimmer, K. Der Diabetes Mellitus. Small 8vo. Liepsic, 1871.
Zolling, G. A. De Diabete. 8vo. Berlin, 1822.

INDEX.

125 mg